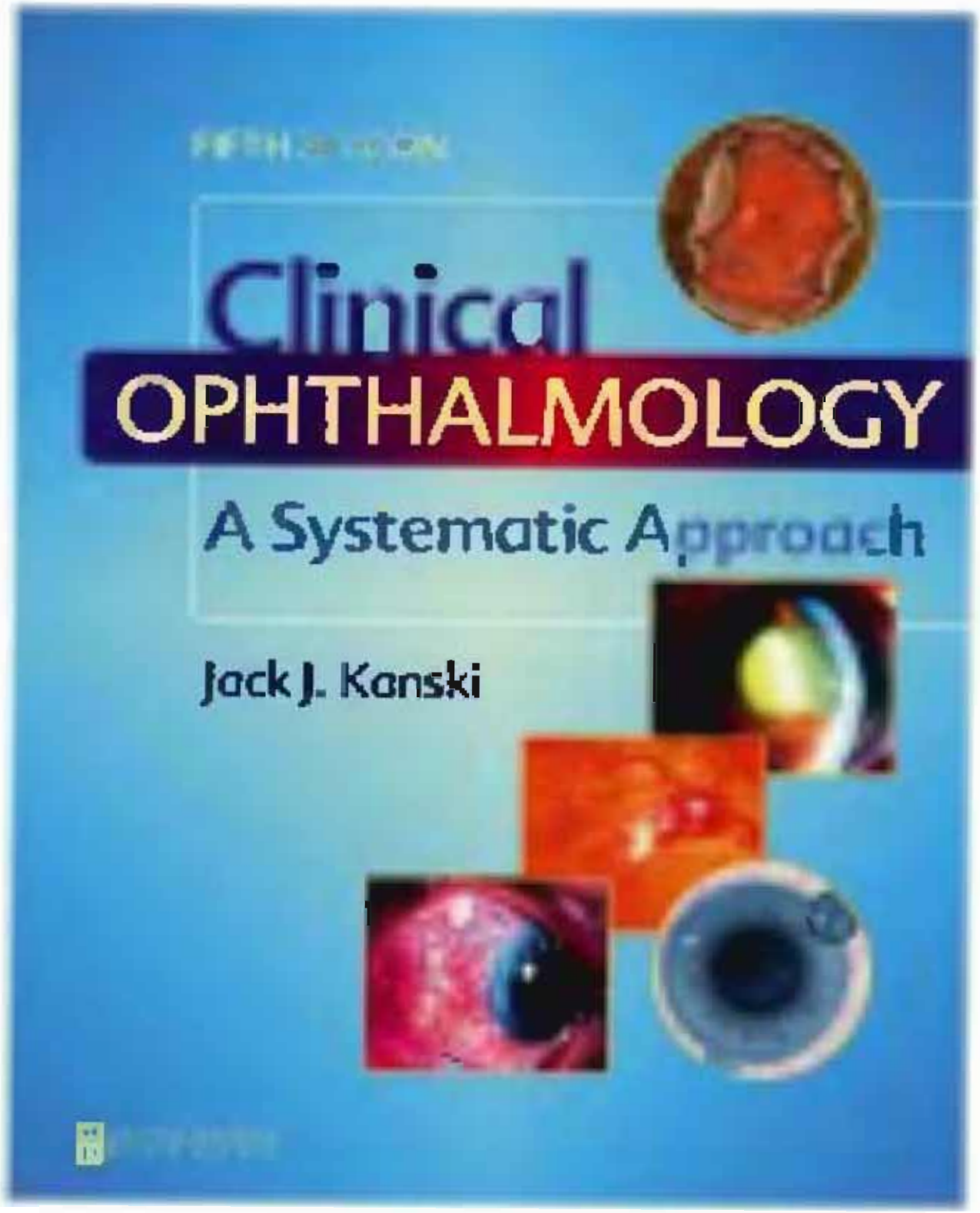
Clinical
OPHTHALMOLOGY
A Systematic Approach
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CHAPTER 1

Eyelids

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Applied anatomy

1. **The grey line** is an important structure because it divides the eyelids into an anterior lamella, composed of skin and orbicularis, and a posterior lamella consisting of tarsal plate and conjunctiva (Fig. 1.1).
2. **Glands** in the lid margin may be the source of cyst formation and occasionally tumours.
   *a. **Meibomian glands*** are modified sebaceous glands located in the tarsal plate and secrete the outer lipid layer of the precorneal tear film.
   *b. **Glands of Zeis*** are modified sebaceous glands that are associated with lash follicles.
   *c. **Glands of Moll*** are modified sweat glands the ducts of which open either into a lash follicle or directly onto the anterior lid margin between the lashes.
3. **The lashes** are slightly more numerous in the upper (approximately 100) than in the lower lid. The lash roots lie against the anterior surface of the tarsus in the space between the pretarsal orbicularis oculi muscle and the muscle of Riolan. The lashes pass between the orbicularis oculi and the muscle of Riolan and exit the skin at the anterior lid margin. All lashes curve away from the globe and are relatively parallel. Because they lack erectores pilorum muscles, their position and direction are determined by the surrounding orbicularis oculi, muscle of Riolan and tarsal plate. Thus, if the tarsus or orbicularis is abnormal, lash position and direction may be affected.
4. **Upper lid elevators** (Fig. 1.2)
   *a. **The levator aponeurosis*** fuses with the orbital septum about 4 mm above the superior border of the tarsus. Its posterior fibres insert into the lower third of the anterior surface of the tarsus. The medial and lateral horns are expansions which act as check ligaments. Surgically, the aponeurosis can be approached through the skin or the conjunctiva.

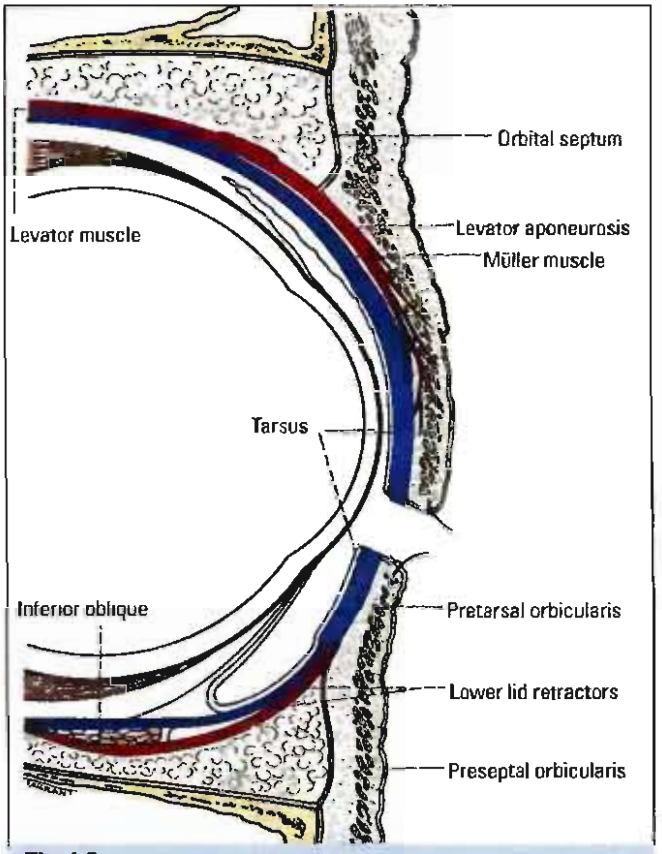

Fig. 1.2
Anatomy of the levator complex and lower lid retractors

   *b. **Müller muscle*** is inserted into the upper border of the tarsus and can be approached transconjunctivally.
5. **Lower lid retractors**
   *a. **The inferior tarsal aponeurosis*** consists of the capsulopalpebral expansion of the inferior rectus muscle and is analogous to the levator aponeurosis.

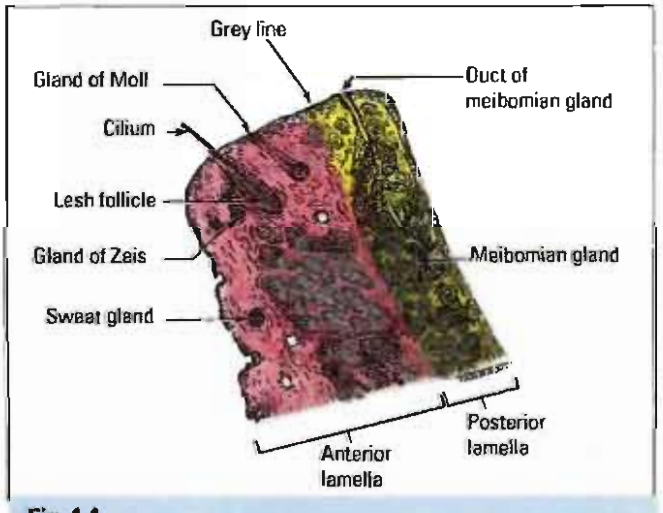

Fig. 1.1
Cross-section of the lower lid

Fig. 1.3
Lymphatic drainage of the lids

b. The inferior tarsal muscle is analogous to Müller muscle.

6. **Lymphatic drainage** (Fig. 1.3). The upper lid and lateral canthus drain into the preauricular nodes, whereas the lower lid and medial canthus drain into the submandibular nodes.

Disorders of lashes

Trichiasis

Trichiasis is a very common acquired condition which may occur in isolation or as a result of scarring of the lid margin secondary to chronic blepharitis, herpes zoster ophthalmicus and trachoma. Trichiasis should not be mistaken for pseudotrichiasis secondary to entropion because in some cases the inturning of the eyelid may be intermittent and the condition may be mistaken for true trichiasis and inappropriately treated.

Signs

Posterior misdirection of lashes arising from normal sites of origin (Fig. 1.4). Trauma to the corneal epithelium may cause punctate epithelial erosions and ocular irritation made worse on blinking. Corneal ulceration and pannus formation may occur in severe long-standing cases.

Treatment

1. **Epilation** with forceps is simple and effective but recurrences within 4–6 weeks are inevitable.
2. **Electrolysis** is useful for a few isolated lashes but is tedious and frequently multiple treatments are required to obtain a satisfactory result. An electrocautery needle is inserted down the shaft of the lash root and current applied until coagulated tissue bubbles to the surface (Fig. 1.5). The lash is then removed. Retreatment for recurrences is required in about 40% of cases and can cause scarring.
3. **Cryotherapy** is very effective in eliminating many lashes (Fig. 1.6). With a special cryoprobe a double freeze–thaw cycle at −20°C is applied. Potential complications include skin necrosis, depigmentation in dark-skinned individuals, damage to meibomian glands, which may adversely affect the precorneal tear film, and shallow notching of the lid margin.
4. **Argon laser ablation** is useful for a few scattered lashes and is performed as follows:
   a. The initial settings are 50 μm, 0.2 seconds and 1000 mW.
   b. The laser is fired at the root of the lash and a small crater formed.

Fig. 1.4
Trichiasis

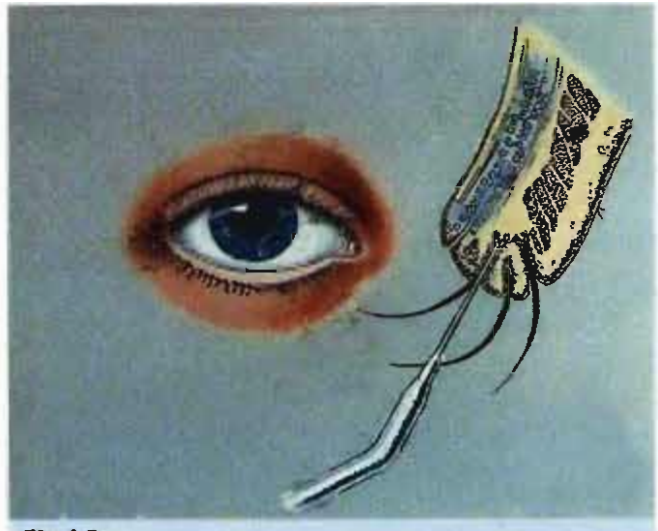

Fig. 1.5
Treatment of trichiasis by electrolysis (Courtesy of Wilmer Institute)

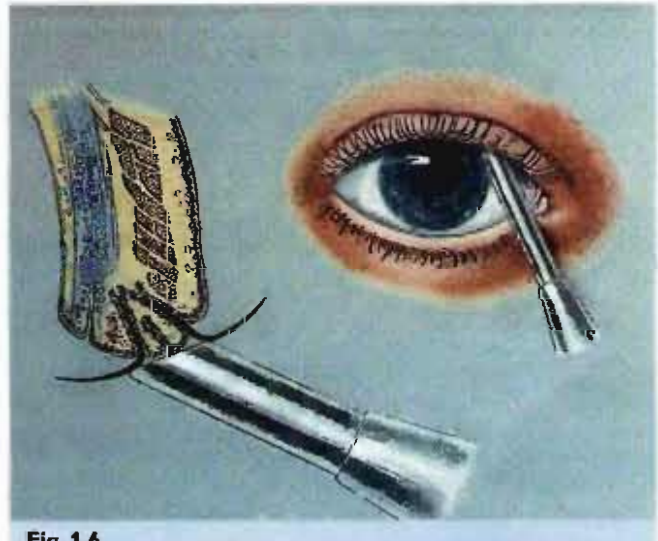

Fig. 1.6
Treatment of trichiasis by cryotherapy (Courtesy of Wilmer Institute)

Fig. 1.7
Appearance following laser ablation of trichiasis

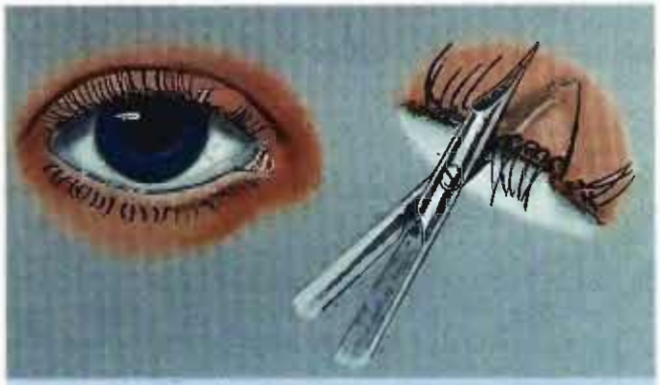

Fig. 1.8
Treatment of trichiasis by full-thickness wedge resection (Courtesy of Wilmer Institute)

Fig. 1.9
Congenital distichiasis

c. The spot size is increased to 200 μm and the crater deepened to reach the follicle (Fig. 1.7).
d. About a dozen applications are required and most patients are cured by either one or two sessions.

5. **Surgery** involving full-thickness wedge resection (Fig. 1.8) or anterior lamellar excision may be useful for a localized crop of lashes resistant to other methods of treatment. More generalized trichiasis requires anterior lamellar reposition surgery.

Congenital distichiasis

Congenital distichiasis is a rare condition which may be sporadic or dominantly inherited. A minority of patients also manifest chronic lymphoedema, spinal arachnoid cysts and congenital heart defects (*lymphoedema–trichiasis syndrome*).

Signs

A partial or complete second row of lashes emerging at or slightly behind the meibomian gland orifices. The aberrant lashes tend to be thinner, shorter and less pigmented than normal cilia and are often directed posteriorly (Fig. 1.9).

Treatment

Treatment involves lamellar eyelid division and cryotherapy.

a. An incision is made along the grey line dividing the lid into anterior and posterior lamellae.
b. The posterior lamella and lash follicles are frozen with a double freeze–thaw cycle to –20°C (Fig. 1.10).
c. The lamellae are surgically re-apposed.

Fig. 1.10
Treatment of distichiasis by cryotherapy (Courtesy of Wilmer Institute)

Acquired distichiasis

Acquired distichiasis (metaplastic lashes) is caused by metaplasia and dedifferentiation of the meibomian glands to become hair follicles. The most important cause is late-stage cicatrizing conjunctivitis associated with chemical

Fig. 1.11
Acquired distichiasis (metaplastic lashes)

injury, Stevens–Johnson syndrome and ocular cicatricial pemphigoid.

1. **Signs**. Variable number of lashes which originate from meibomian gland orifices (Fig. 1.11).
2. **Treatment** of mild cases is as for trichiasis. Severe cases require lamellar eyelid division and cryotherapy to the posterior lamella.

Phthiriasis palpebrarum

The crab louse *Phthirus pubis* is adapted to living in pubic hair. An infested person may transfer the lice to another hairy area such as the chest, axilla or eyelid. Phthiriasis palpebrarum is an infestation of the lashes which typically affects children living in poor hygienic conditions and causes chronic irritation and itching.

Signs

The lice are anchored to the lashes by their thick claws (Fig. 1.12). The ova and their empty shells appear as oval, brownish, opalescent pearls adherent to the base of the cilia.

Fig. 1.12
Lice and nits clinging to the lashes in phthiriasis palpebrarum

Treatment

1. **Trimming of lashes** at their bases results in immediate mechanical removal of the lice and ova. It also destroys the hair-shaft habitat for louse survival and reproduction.
2. **Destruction** of lice and ova with topical application of yellow mercuric oxide 1% or anticholinesterase agents, laser or cryotherapy, if trimming is undesirable.
3. **Delousing** of the patient, other family members, clothing and bedding to prevent recurrences.

Poliosis

Poliosis is a premature localized whitening of hair which may involve the lashes and eyebrows (Fig. 1.13). The main causes are shown in Table 1.1.

Fig. 1.13
Poliosis of lashes

Table 1.1 Causes of poliosis

1. **Ocular**
   - chronic anterior blepharitis
   - sympathetic ophthalmitis
2. **Systemic**
   - Vogt–Koyangi–Harada syndrome
   - Waardenburg syndrome

Madarosis

Madarosis is a decrease in number or complete loss of lashes (Fig. 1.14). The main causes are shown in Table 1.2.

Hypertrichosis

Hypertrichosis is an excess number of lashes (polytrichosis) and/or abnormally long and luxuriant lashes (trichomegaly)

Fig. 1.14
Madarosis

Fig. 1.15
Hypertrichosis

Table 1.2 Causes of madarosis

1. **Local**
   - chronic anterior lid margin disease
   - infiltrating tumours
   - burns
   - radiotherapy or cryotherapy of lid tumours
2. **Skin disorders**
   - generalized alopecia
   - psoriasis
3. **Systemic disorders**
   - myxoedema
   - systemic lupus erythematosus
   - acquired syphilis
   - lepromatous leprosy
4. **Following removal**
   - iatrogenic for trichiasis
   - trichotillomania—psychiatric disorder of habitual hair removal

(Fig. 1.15). The condition may be congenital or drug-induced (e.g. phenytoin, cyclosporin and latanoprost).

Eyelash ptosis

Eyelash ptosis is a downward displacement of lashes (Fig. 1.16). The condition may be idiopathic or associated with the floppy eyelid syndrome, dermatochalasis with anterior lamellar slip or long-standing facial palsy.

Fig. 1.16
Eyelash ptosis

Fig. 1.17
Acute allergic oedema

Allergic disorders

Acute allergic oedema

Acute allergic oedema is usually caused by insect bites, angioedema and urticaria, and occasionally drugs.

1. **Signs.** Sudden onset of painless, pitting periorbital and lid oedema (Fig. 1.17).
2. **Treatment** with systemic antihistamines may be helpful.

Fig. 1.18
Contact dermatitis

Contact dermatitis

Contact dermatitis is caused by sensitivity to topical medication, either to the active component or the preservative. Common causes include neomycin, chloramphenicol and dorzolamide.

1. **Signs.** Lid swelling and erythema associated with tearing and itching. If the cause is not withdrawn the oedema lessens but the erythema persists and the skin becomes thickened and crusty (Fig. 1.18).
2. **Treatment** involves identification and removal of the cause and short-term application of a cream containing a mild steroid such as hydrocortisone 1%.

Atopic dermatitis

Atopic dermatitis (eczema) is a very common, idiopathic condition frequently associated with asthma and hay fever.

Fig. 1.19
Atopic dermatitis

Eyelid involvement is relatively infrequent but when present is invariably associated with generalized dermatitis.

1. **Signs.** Thickening, crusting and vertical fissuring of the lids associated with staphylococcal blepharitis and madarosis (Fig. 1.19).
2. **Treatment** is with emollients to hydrate the skin and the judicious use of mild topical steroids such as hydrocortisone 1%. It is also important to treat associated infection.
3. **Ocular associations**
   a. Common. Vernal disease in children and chronic keratoconjunctivitis in adults.
   b. Uncommon. Keratoconus, presenile cataract and retinal detachment.

Infections

Herpes zoster ophthalmicus

Herpes zoster ophthalmicus is a common, unilateral infection caused by varicella-zoster virus. It typically affects the elderly but may occur at an earlier age and be more severe in immunocompromised individuals.

Clinical features

1. **Presentation** is with pain in the distribution of the first division of the trigeminal nerve.
2. **Signs** (in chronological order)
   - A maculopapular rash on the forehead.
   - Progression through vesicles, pustules to crusting ulceration.

Fig. 1.20
Bilateral oedema due to unilateral herpes zoster ophthalmicus

- Periorbital oedema may spread to the other side, giving the erroneous impression that the condition is bilateral (Fig. 1.20).
- Ocular complications (*see* Chapter 5).

Treatment

1. **Systemic** treatment is for 7 days with valaciclovir 1 g t.i.d. or famciclovir 250 mg t.i.d. or 750 mg once daily.
2. **Topical** aciclovir or penciclovir cream, and a steroid–antibiotic combination such as Fucidin-H (hydrocortisone 1%, fucidic acid 2%) or Terra-Cortil (hydrocortisone 1%, oxytetracycline 3%). These should be used t.i.d. until the crusts have separated.

NB: Talc and calamine lotion should be avoided.

Herpes simplex

Primary herpes simplex infection is an uncommon, unilateral condition which typically affects children. It may be particularly severe in patients with associated atopic dermatitis or immunodeficiency states.

1. **Signs.** Crops of small vesicles which rupture, crust and heal within a few days (Fig. 1.21). Uncommon complications include ipsilateral follicular conjunctivitis and keratitis.
2. **Treatment** is with aciclovir or penciclovir cream, taking care to avoid contact with the eyes.

Fig. 1.21
Vesicles due to primary herpes simplex infection

Impetigo

Impetigo is an uncommon, superficial skin infection caused by *Staph. aureus* or *Strep. pyogenes* which most frequently affects children. Involvement of the eyelids is usually associated with painful infection of the face.

1. **Signs.** Erythematous macules which rapidly develop into vesicles and bullae which produce golden-yellow crusts on rupturing (Fig. 1.22).

Fig. 1.22
Impetigo

2. **Treatment** is with topical antibiotics and oral flucloxacillin or erythromycin.

Erysipelas

Erysipelas (St Anthony fire) is an uncommon, acute subcutaneous spreading cellulitis usually caused by *Strep. pyogenes* through a site of minor skin trauma.

1. **Signs.** An expanding, well-defined, indurated, erythematous, subcutaneous plaque (Fig. 1.23). Primary lid involvement, when it occurs, is usually severe and may result in secondary contracture.
2. **Treatment** is with oral phenoxymethylpenicillin.

Fig. 1.23
Erysipelas due to minor skin trauma

Fig. 1.24
Gangrene due to necrotizing fasciitis

Necrotizing fasciitis

Necrotizing fasciitis is an extremely rare rapidly progressive necrosis initially involving subcutaneous soft tissues and later usually the skin which is usually caused by *Strep. pyogenes* and occasionally by *Staph. aureus*. The most frequent sites of involvement are the extremities, trunk and perineum, as well as postoperative wound sites. Unless treatment is early and appropriate, death may result. Periocular infection is rare and may be secondary to trauma or surgery.

1. **Signs**. Periorbital redness and oedema leading to formation of large bullae and black discoloration of skin due to gangrene secondary to underlying thrombosis (Fig. 1.24).
2. **Complications** include ophthalmic artery occlusion, lagophthalmos and disfigurement.
3. **Treatment** is with intravenous benzylpenicillin, debridement of necrotic tissue and reconstructive surgery.

Chronic marginal blepharitis

Pathogenesis

The pathogenesis of anterior blepharitis is unclear although both staphylococcal infection and seborrhoea play important roles (Table 1.3).

1. **Seborrhoeic blepharitis** is usually associated with seborrhoeic dermatitis which may involve the scalp, nasolabial folds, retroauricular areas and sternum. It has been postulated that excessive neutral lipids are broken down by *Corynebacterium acnes* into irritating fatty acids.
2. **Posterior blepharitis** is manifest as meibomian gland dysfunction (ocular rosacea) which may be associated with facial rosacea (*see* Chapter 20).

NB: Because of the intimate relationship between the lids and ocular surface, chronic blepharitis may cause secondary changes in the conjunctiva and cornea.

Table 1.3 Classification of chronic blepharitis

1. **Anterior**
   - staphylococcal
   - seborrhoeic
   - mixed
2. **Posterior**
   - meibomian seborrhoea
   - meibomianitis
3. **Mixed anterior and posterior**

Anterior blepharitis

Clinical features

1. **Symptoms** include burning, grittiness, mild photophobia, and crusting and redness of the lid margins. These are usually worse in the mornings and are characterized by remissions and exacerbations. Surprisingly there is frequently little correlation between severity of symptoms and extent of clinical involvement.
2. **Signs**
   a. ***Staph. blepharitis*** is characterized by hyperaemia and telangiectasia of the anterior lid margins with hard scales mainly located around the bases of the lashes (collarettes) (Figs 1.25 and 1.26).
   b. ***Seborrhoeic blepharitis*** is characterized by hyperaemic and greasy anterior lid margins with sticking together of lashes (Fig. 1.27). The scales are soft and located anywhere on the lid margin and lashes (Fig. 1.28).
   c. ***Severe long-standing*** anterior blepharitis, particularly staphylococcal, may result in hypertrophy and scarring of the lid margin, madarosis (Fig. 1.29), trichiasis and poliosis (Fig. 1.30).

Fig. 1.25
Telangiectasia of the anterior lid margin and scales in staphylococcal blepharitis

Fig. 1.26
Hard scales in staphylococcal blepharitis

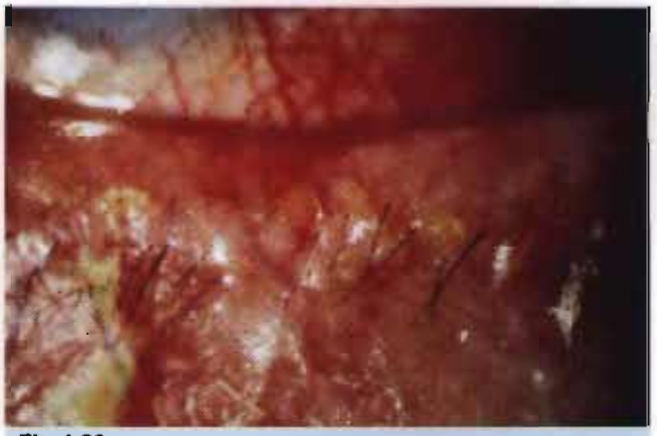

Fig. 1.29
Notching, scarring and madarosis in long-standing staphylococcal blepharitis

Fig. 1.27
Greasy lashes in seborrhoeic blepharitis

Fig. 1.30
Trichiasis and poliosis in long-standing staphylococcal blepharitis

Fig. 1.28
Greasy lashes and scales in seborrhoeic blepharitis

3. Associations

- External hordeola (styes) may develop by spread of infection to the glands of Moll or Zeis.
- Tear film instability is present in 30–50% of cases.
- Hypersensitivity to staphylococcal exotoxins may result in papillary conjunctivitis, inferior corneal epithelial punctate erosions and marginal keratitis.

Treatment

This is tedious and patients should be advised that despite the lack of permanent cure control of symptoms is usually possible. In long-standing cases several weeks of intensive treatment may be necessary to achieve improvement.

1. **Lid hygiene** to remove crusts and toxic products involves scrubbing the lid margins daily with a commercially availabla lid scrub, a cotton bud dipped in a 25% solution of baby shampoo or a weak solution of sodium bicarbonate. Alternatively a face cloth or handkerchief can be used. It is also useful to scrub the eyelids with diluted shampoo when washing the hair. Gradually, lid hygiene can be performed less frequently as the condition is brought under control but must not be stopped or the blepharitis will recur.
2. **Antibiotic ointment** such as sodium fusidate (Fucidin) or chloramphenicol is used to treat acute folliculitis but is

Fig. 1.31
Sebaceous gland carcinoma causing localized loss of lashes and mimicking chronic blepharitis

of limited value in long-standing cases. Following lid hygiene the ointment should be rubbed onto the anterior lid margin with a cotton bud or clean finger.

3. **Weak topical steroids** such as fluorometholone administered short term q.i.d. are useful for secondary papillary conjunctivitis and marginal keratitis.
4. **Tear substitutes** are required for associated tear film instability. Unless this aspect of the disease is recognized and treated relief of symptoms will be incomplete.

Differential diagnosis

1. **Dry eye** can cause similar symptoms, but in contrast to blepharitis, ocular irritation is seldom severe in the morning and usually develops later in the day.
2. **Infiltrating lid tumours** should be suspected in patients with apparently asymmetrical or unilateral chronic blepharitis, particularly when associated with madarosis (Fig. 1.31).

Posterior blepharitis

Meibomian seborrhoea

This is characterized by excessive meibomian gland secretions. It is easy to miss because symptoms may be severe but clinical signs of blepharitis are mild.

1. **The meibomian gland orifices** are capped by small oil globules (Fig. 1.32). Pressure on the tarsus results in expression of copious amounts of meibomian oil.
2. **The tear film** is oily and foamy, and in severe cases froth accumulates on the lid margins or inner canthi (meibomian foam) (Fig. 1.33).

Meibomianitis

This is characterized by inflammation and obstruction of the meibomian glands.

1. **The posterior lid margin** shows hyperaemia, telangiectasia and obstruction of meibomian gland orifices (Figs 1.34 and 1.35). Long-standing cases are charac-

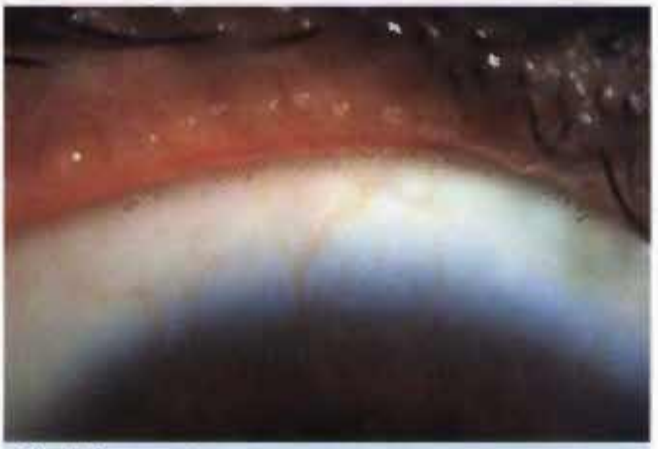

Fig. 1.32
Capping of meibomian gland orifices with oil in posterior blepharitis

Fig. 1.33
Foam in meibomian seborrhoea

Fig. 1.34
Diffuse inflammation around meibomian gland orifices in meibomianitis

terized by cystic dilatation of meibomian ducts, with thickening and notching of the lid margin (Fig. 1.36).

2. **Expressed meibomian gland secretions** in long-standing cases may be turbid or inspissated, appearing as toothpaste-like plaques (Fig. 1.37). In very severe cases no secretions can be expressed.

Complications

- Chalazion formation, which may be recurrent (Fig. 1.38).
- Tear film instability in about 30% of patients. This is probably the result of imbalance between the aqueous and lipid components of the tear film, allowing increased evaporation and dryness.
- Papillary conjunctivitis and inferior corneal epithelial erosions.

Treatment

1. **Systemic tetracyclines** are the mainstay of treatment but should not be used in children under the age of 12 years or in pregnant or breast-feeding women because they are deposited in growing bone and teeth (being bound to calcium), and may cause staining of teeth and dental hypoplasia. One of the following preparations may be used:
   - Tetracycline 250 mg q.i.d. for 1 week and then b.d. for 6–12 weeks.
   - Doxycycline 100 mg b.d. for 1 week and then daily for 6–12 weeks.
   - Minocycline 100 mg daily for 6–12 weeks.
2. **Erythromycin** or azithromycin may be used when tetracyclines are contraindicated, but their efficacy in posterior blepharitis is not well established.
3. **Other measures**
   - Lid hygiene, weak topical steroids and tear substitutes as for anterior blepharitis.
   - Warm compresses to melt solidified sebum and mechanical expression of the meibomian glands to reduce the amount of irritating lipids within the glands.
   - Topical sodium fusidate gel in patients with associated acne rosacea.

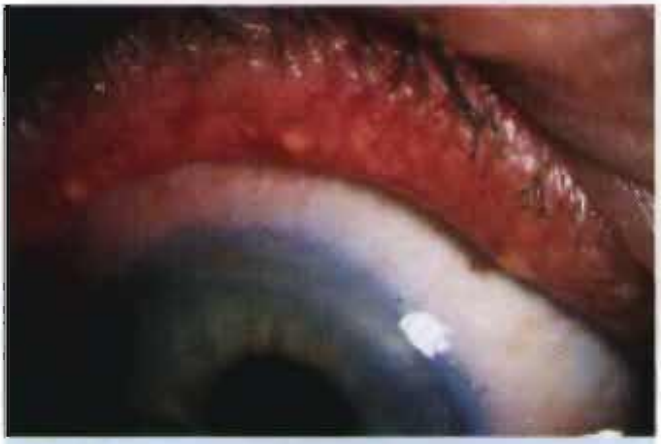

Fig. 1.35
Blocked meibomian gland orifices and scarring of the posterior lid margin in long-standing posterior blepharitis

Fig. 1.36
Obstruction of meibomian glands and telangiectasia of the posterior lid margin in long-standing posterior blepharitis

Fig. 1.37
Toothpaste-like plaques expressed from meibomian glands in posterior blepharitis

Fig. 1.38
Small chalazia associated with posterior blepharitis

Benign nodules and cysts

Chalazion

A chalazion (meibomian cyst) is a chronic, sterile, lipogranulomatous inflammatory lesion caused by blockage of meibomian gland orifices and stagnation of sebaceous secretions. Patients with acne rosacea or seborrhoeic dermatitis are at increased risk of chalazion formation, which may be multiple or recurrent.

Clinical features

1. **Presentation** is at any age with a gradually enlarging painless nodule. Occasionally an upper lid chalazion may press on the cornea, induce astigmatism and cause blurred vision.
2. **Signs**. A non-tender, roundish, firm lesion within the tarsal plate of variable size which may be multiple or bilateral (Fig. 1.39). Eversion of the lid may show an associated polypoidal granuloma if the lesion has ruptured through the tarsal conjunctiva (Fig. 1.40).

Fig. 1.39
Chalazion

Fig. 1.40
Conjunctival granuloma associated with a chalazion

Fig. 1.41
Incision of chalazion

Treatment

Small chalazia may occasionally disappear spontaneously. Persistent lesions may be treated as follows:

1. **Surgery**. The eyelid is everted with a special clamp, the cyst is incised vertically and its contents curetted through the tarsal plate (Fig. 1.41). It is very important not to mistake a sebaceous gland carcinoma for a 'recurrent chalazion'. In doubtful cases, the lesion should be biopsied and examined histologically.
2. **Steroid injection** into the lesion. Between 0.1 and 0.2 ml triamcinolone diacetate aqueous suspension diluted with lignocaine (or equivalent) to a concentration of 5 mg/ml is injected through the conjunctiva with a 30-gauge needle. The success rate following one injection is about 80%. In unresponsive cases a second injection can be given 2 weeks later.
3. **Systemic tetracycline** may be required as prophylaxis in patients with recurrent chalazia, particularly if associated with acne rosacea or seborrhoeic dermatitis.

Internal hordeolum

An internal hordeolum is an abscess caused by an acute staphylococcal infection of a meibomian gland.

1. **Signs**. A tender, painful swelling within the tarsal plate (Fig. 1.42). The lesion may enlarge and then discharge either posteriorly through the conjunctiva or anteriorly through the skin.
2. **Treatment** by incision and curettage may be required if a residual nodule remains after the acute infection has subsided.

Fig. 1.42
Large internal hordeolum about to discharge

External hordeolum

An external hordeolum (stye) is an acute staphylococcal abscess of a lash follicle and its associated gland of Zeis or Moll which usually affects children.

1. **Signs**. A tender swelling in the lid margin pointing anteriorly through the skin (Fig. 1.43). Multiple lesions may be present and occasionally minute abscesses may involve the entire lid margin.
2. **Treatment** with hot compresses and epilation of the lash associated with the infected follicle may hasten resolution.

Molluscum contagiosum

Molluscum contagiosum is a skin infection caused by a poxvirus which typically affects otherwise healthy children. Immunocompromised patients, however, may have atypical multiple and frequently confluent lesions which are more resistant to treatment than in healthy individuals.

1. **Signs**. Pale, waxy, umbilicated nodule (Fig. 1.44).

> *NB:* Patients may occasionally present with a secondary ipsilateral chronic follicular conjunctivitis and unless the lid margin is examined carefully the causative molluscum lesion may be overlooked.

Fig. 1.43
External hordeolum (stye)

Fig. 1.44
Molluscum contagiosum

2. **Treatment** may not be necessary unless the lesion is very close to the lid margin. Treatment options include shave excision or destruction of the lesion by cauterization, cryotherapy or laser.

Xanthelasma

Xanthelasma is a common, frequently bilateral condition which is usually found in middle-aged and elderly patients or those with hyperlipidaemia.

1. **Signs**. Yellowish, subcutaneous plaques consisting of cholesterol and lipid which are usually located at the medial aspects of the eyelids (Fig. 1.45).
2. **Treatment** for cosmetic reasons is either by excision or, preferably, destruction with a carbon dioxide or argon laser.

Cyst of Moll

A cyst of Moll (apocrine sweat gland hidrocystoma) is a small, round, non-tender, translucent fluid-filled lesion on the anterior lid margin (Fig. 1.46).

Fig. 1.45
Xanthelasma

Fig. 1.46
Cyst of Moll

Fig. 1.47
Large eccrine sweat gland hidrocystoma at the outer canthus and a cyst of Moll on the upper lid

Fig. 1.48
Cyst of Zeis

Eccrine sweat gland hidrocystoma

An eccrine sweat gland hidrocystoma is less common but similar in appearance to a cyst of Moll, except that it is not confined to the lid margin (Fig. 1.47).

Cyst of Zeis

A cyst of Zeis contains oily secretions and is therefore less translucent than a cyst of Moll (Fig. 1.48).

Sebaceous cyst

A sebaceous cyst arises from an ordinary sebaceous gland and is characterized by a central punctum with retained cheesy secretions. It is rarely found on the eyelid although it may occur at the inner canthus (Fig. 1.49).

Milia

Milia are tiny, white, round, superficial cysts which tend to occur in crops (Fig. 1.50). They are derived from hair follicles or sebaceous glands.

Fig. 1.49
Sebaceous cysts

Fig. 1.50
Milia

Benign tumours

Viral wart

A viral wart (squamous cell papilloma) is the most common benign tumour of the eyelids which is usually found in adults.

1. **Signs**. A pedunculated or broad-based (sessile) lesion with a characteristic raspberry-like surface (Fig. 1.51).
2. **Treatment** involves excision or laser ablation.

Seborrhoeic keratosis

Seborrhoeic keratosis (basal cell papilloma) is a common, slow-growing condition found on the face and eyelids of elderly individuals.

1. **Signs**. A discrete, greasy, brown, flat, round or oval lesion with a friable verrucous surface and a 'stuck-on' appearance (Fig. 1.52). Occasionally the lesion may be pedunculated.

Fig. 1.51
Pedunculated viral wart

Fig. 1.52
Seborrhoeic keratosis

2. **Treatment** involves curettage of small flat lesions and excision of pedunculated lesions.

Actinic keratosis

Actinic (solar) keratosis is the most common pre-malignant skin lesion but rarely develops on the eyelids. It typically affects elderly, fair-skinned individuals who have been exposed to excessive sunlight and most frequently occurs on the forehead and backs of the hands.

1. **Signs**. A flat, scaly, hyperkeratotic lesion (Fig. 1.53). Occasionally the lesion is nodular or wart-like and may be associated with a cutaneous horn.
2. **Treatment** involves biopsy to confirm the diagnosis, followed by either excision or cryotherapy.

Cutaneous horn

A cutaneous horn is an uncommon lesion which is occasionally associated with underlying actinic keratosis or squamous cell carcinoma.

1. **Signs**. A hyperkeratotic lesion protruding through the skin (Fig. 1.54).
2. **Treatment** involves biopsy to determine the underlying pathology, followed by excision.

Pyogenic granuloma

A pyogenic granuloma is a fast-growing vascularized proliferation of granulomatous tissue which is usually antedated by surgery, trauma or infection, although some cases are idiopathic.

1. **Signs.** A pinkish, pedunculated or sessile mass which may bleed following relatively trivial trauma (Fig. 1.55).
2. **Treatment** is by excision.

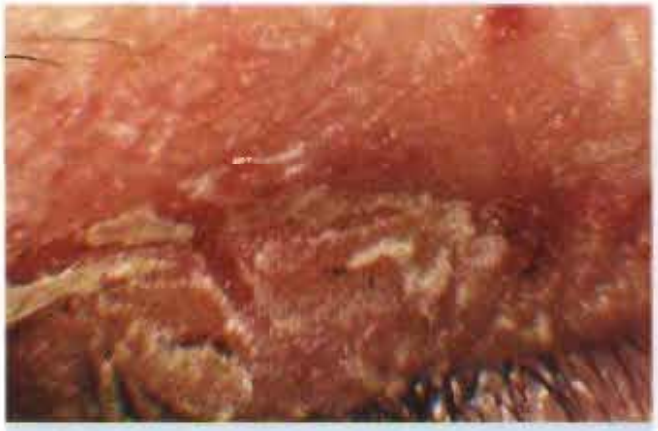

Fig. 1.53
Actinic keratosis

Fig. 1.54
Cutaneous horn

Fig. 1.56
Pigmented intradermal naevus

Fig. 1.55
Pyogenic granuloma

Fig. 1.57
'Kissing naevi' (Courtesy of S. Webber)

Melanocytic naevus

A melanocytic naevus is composed of atypical melanocytes (naevus cells). The clinical appearance, classification and potential for malignant transformation of naevi are determined by their histological location within the skin as follows:

1. **Intradermal naevus**, the most common, is usually elevated and frequently has a papillomatous configuration (Fig. 1.56). It may be non-pigmented or brown-black in colour. When located on the eyelid margin, lashes may grow through the lesion. Occasionally symmetrical lesions may be present on adjacent portions of the upper and lower lids ('kissing naevi') (Fig. 1.57). Histologically the naevus cells are confined to the dermis and have no malignant potential.
2. **Junctional naevus** is usually flat, well circumscribed and uniformly brown in colour (Fig. 1.58). The naevus cells are located at the junction of the epidermis and dermis and have a low potential for malignant transformation.
3. **Compound naevus** has both intradermal and junctional components and is usually brown. It has a low malignant potential which is related to the junctional component.

Fig. 1.58
Pigmented junctional naevus

Keratoacanthoma

Keratoacanthoma is an uncommon, benign but rapidly growing tumour which usually occurs in otherwise healthy fair-skinned individuals with a history of chronic sun

exposure. It is found more frequently than would be expected by chance in patients on immunosuppressive therapy following renal transplants. Keratoacanthoma may have a clinically similar appearance to squamous cell carcinoma, particularly in immunosuppressed individuals. Histopathologically keratoacanthoma is regarded as part of the spectrum of squamous cell carcinoma, into which it may evolve.

1. **Signs** (in chronological order)
   - A pink papule which may double or treble in size within a few days.
   - The lesion generally stops growing and remains static for 2–3 months, after which time it starts to involute spontaneously.
   - At the end of the growth phase the lesion is a firm, dome-shaped nodule (Fig. 1.59).
   - During the period of regression the central part of the lesion becomes hyperkeratotic and a keratin-filled crater may develop (Fig. 1.60).
   - Complete involution may take up to a year and usually leaves a residual ugly scar.
2. **Treatment** is by excision, especially if there is no sign of spontaneous involution.

Fig. 1.59
Keratoacanthoma

Fig. 1.60
Keratoacanthoma with a keratin-filled crater

Strawberry naevus

Strawberry naevus (capillary haemangioma) although rare is one of the most common tumours of infancy and presents shortly after birth. The female to male ratio is 3:1 and occasionally the tumour is familial. Eyelid angiomas have a predilection for the upper lid and may have orbital extensions. Occasionally the lesion may also involve the skin of the face (Fig. 1.61) and some patients have strawberry naevi on other parts of the body. It is important to be aware of the association between multiple cutaneous lesions and visceral haemangiomas.

Signs (in chronological order)

- A unilateral, raised, red lesion which blanches with pressure and may swell on crying (Fig. 1.62). A large tumour on the upper lid may cause mechanical ptosis (Fig. 1.63).

Fig. 1.61
Extensive capillary haemangioma

Fig. 1.62
Small capillary haemangioma

Fig. 1.63
Large capillary haemangioma

- The tumour usually grows quickly during the first year of life and stops growing during the second year.
- At about the age of 2 years the tumour begins to involute spontaneously with complete resolution occurring in 40% of patients by the age of 4 years and 70% by age 7.

Systemic associations

A small minority of patients with very large fast-growing naevi may have the following:

a. ***Kasabach–Merritt syndrome***, which is characterized by thrombocytopenia, anaemia and low levels of coagulant factors.

b. ***Maffuci syndrome***, which is characterized by skin haemangiomas, enchondromata of hands, feet and long bones as well as bowing of long bones.

Treatment

Treatment is indicated when vision is threatened by amblyopia as a result of anisometropia, ptosis or strabismus.

1. **Laser** treatment to close blood vessels in very early lesions.
2. **Injection** of steroid into the tumour is the most frequently used method. The injection contains a mixture, in equal parts, of triamcinolone acetonide 40 mg/ml and betamethasone 4 mg/ml. The tumour usually begins to regress within 2 weeks but, if necessary, second and third injections can be given after about 2 months. Potential complications are skin depigmentation, fat atrophy, eyelid necrosis and rarely occlusion of the central retinal artery.
3. **Systemic** steroids for extensive lesions, particularly if associated with visceral involvement.
4. **Subcutaneous** injection of interferon alpha-2b is a good option for the treatment of steroid-resistant, organ-interfering and/or life-threatening giant haemangiomas.
5. **Surgical resection** may be appropriate in selected cases.

Port-wine stain

A port-wine stain (naevus flammeus) is a rare congenital, subcutaneous cavernous haemangioma which most frequently occurs on the face. The lesion is usually unilateral and segmental but may be bilateral.

1. **Signs** (in chronological order)
   - A sharply demarcated, soft, pink patch which does not blanch with pressure (Fig. 1.64a).
   - With age, the lesion does not grow but darkens to red or purple (Fig. 1.64b).

Fig. 1.64
Progression of skin changes in naevus flammeus. Darkening from red (a) to purple (b); (c) hypertrophy and nodularity

- The overlying skin may become hypertrophied, coarse, nodular and friable and may bleed or become infected (Fig. 1.64c).

2. **Associations** in patients with extensive lesions involving the first and second divisions of the trigeminal nerve are ipsilateral glaucoma (in about 30%), diffuse ipsilateral choroidal haemangioma and Sturge–Weber syndrome in 5% of cases (*see* Chapter 20).
3. **Treatment** with an erbium laser, if undertaken during early life, is effective in decreasing the amount of skin discoloration in relatively flat or mildly hypertrophic lesions.

Malignant tumours

Basal cell carcinoma

General features

Basal cell carcinoma (BCC) is the most common human malignancy, which most frequently affects elderly patients. The most important risk factors are fair skin, inability to tan and chronic exposure to sunlight. Ninety per cent of cases occur in the head and neck and, of these, about 10% involve the eyelid. BCC is by far the most common malignant eyelid tumour, accounting for 90% of all cases. It most frequently arises from the lower eyelid, followed in relative frequency by the medial canthus, upper eyelid and lateral canthus. The tumour is slow growing and locally invasive but non-metastasizing. Tumours located near the medial canthus are more prone to invade the orbit and sinuses, are more difficult to manage than those arising elsewhere and carry the greatest risk of recurrence. Tumours that recur following incomplete treatment tend to be more aggressive and difficult to manage.

Rare predisposing conditions

Young patients who suffer from one of these conditions may develop BCC:

1. **Xeroderma pigmentosum** is an autosomal recessive disease characterized by skin damage on exposure to natural sunlight which gives rise to progressive cutaneous pigmentation abnormalities. Affected patients have a rather bird-like facies and a great propensity to the development of skin BCC as well as squamous cell carcinoma and melanoma, which may be multiple (Fig. 1.65). Conjunctival malignancies have also been reported.
2. **Gorlin–Goltz syndrome** (naevoid basal cell carcinoma syndrome) is a rare autosomal dominant disorder characterized by extensive congenital deformities of the eye, face, bone and CNS. Many patients develop multiple, small BCC during the second decade of life. They are also predisposed to other malignancies including medulloblastoma, breast carcinoma and Hodgkin lymphoma.

Fig. 1.65
Xeroderma pigmentosum and two eyelid basal cell carcinomas

Clinical types

1. **Nodulo-ulcerative** BCC starts as a shiny, firm, pearly nodule with small dilated blood vessels on its surface. Initially, growth is slow and it may take the tumour 1–2 years to reach a diameter of 0.5 cm (Fig. 1.66). If the tumour is not recognized and treated at an early stage, subsequent growth is faster and the lesion develops central ulceration (Fig. 1.67), raised rolled edges with dilated blood vessels over its lateral margins (rodent ulcer) (Fig. 1.68). With time it may erode a large portion of the eyelid (Fig. 1.69).
2. **Sclerosing** BCC (morphoeic) is less common and may be difficult to diagnose because it infiltrates laterally beneath the epidermis as an indurated plaque which may distort the eyelid (Fig. 1.70). The margins of the

Fig. 1.66
Small nodular basal cell carcinoma

Fig. 1.67
Small rodent ulcer

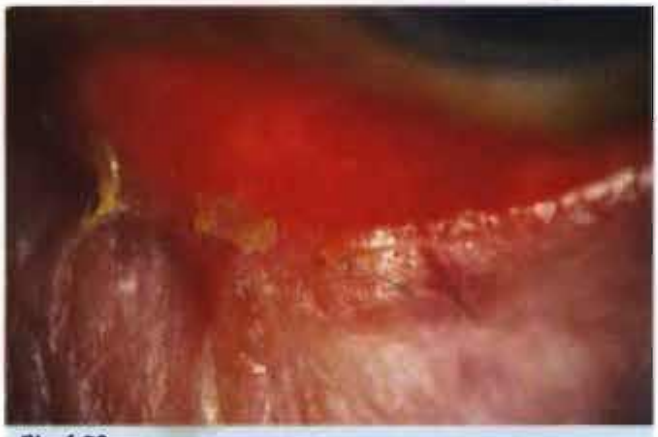

Fig. 1.70
Sclerosing basal cell carcinoma causing mechanical ectropion

Fig. 1.68
Large rodent ulcer

Fig. 1.71
Sclerosing basal cell carcinoma mimicking chronic blepharitis

Fig. 1.69
Erosion of the eyelid by a rodent ulcer

tumour may be impossible to delineate clinically and the lesion tends to be much more extensive on palpation than inspection. On cursory examination a sclerosing BCC may simulate a localized area of unilateral 'chronic blepharitis' (Fig. 1.71).

Squamous cell carcinoma

General features

Squamous cell carcinoma (SCC) is a much less common, but potentially a more aggressive tumour than BCC, with eventual metastasis to regional lymph nodes. There may also be perineural spread to the intracranial cavity via the orbit. SCC accounts for 5–10% of eyelid malignancies and may arise *de novo* or from pre-existing actinic keratosis. Immunocompromised patients with AIDS or following renal transplants are at increased risk. The tumour has a predilection for the lower eyelid and the lid margin. It occurs most commonly in elderly individuals with a fair complexion and a history of chronic sun exposure and skin damage. The diagnosis of SCC may be difficult because certain benign-looking lesions such as keratoacanthoma may reveal histological evidence of invasive SCC at deeper levels of sectioning; conversely other malignant tumours, precancerous lesions and benign tumours may mimic SCC. Clinically, SCC may be indistinguishable from a BCC but it does not usually manifest surface vascularization and grows more rapidly.

Clinical types

1. **Plaque-like** SCC is characterized by a roughened, scaly, erythematous, hyperkeratotic plaque which may arise at the site of pre-existing actinic keratosis (Fig. 1.72).
2. **Nodular** SCC is characterized by a hyperkeratotic nodule which may develop crusting erosions and fissures (Fig. 1.73).
3. **Ulcerating** SCC has a red base and sharply defined, indurated and everted borders (Fig. 1.74).

Fig. 1.72
Plaque-like squamous cell carcinoma (Courtesy of H. Frank)

Fig. 1.73
Nodular squamous cell carcinoma (Courtesy of H. Frank)

Fig. 1.74
Ulcerating squamous cell carcinoma (Courtesy of H. Frank)

Sebaceous gland carcinoma

General features

Sebaceous gland carcinoma (SGC) is a very rare slow-growing tumour which most frequently affects the elderly. It most frequently arises from the meibomian glands, although on occasion it may arise from the glands of Zeis or sebaceous glands. In contrast to BCC and SCC, the tumour occurs more commonly on the upper eyelid, where meibomian glands are more numerous. In about 5% of cases there is simultaneous involvement of both lids on one side, probably due to intra-epithelial spread or spontaneous development of multiple primaries. The clinical diagnosis of SGC is frequently difficult because, in its early stages, external signs of malignancy may be subtle so that the tumour may resemble a less aggressive lesion. As a result of frequent difficulties in diagnosis and delay in treatment, the overall mortality rate is about 10%. Bad prognostic features are upper lid involvement, tumour size of 10 mm or more and a duration of symptoms of over 6 months.

Clinical types

1. **Nodular meibomian gland carcinoma** presents with a discrete, hard nodule most commonly within the upper tarsal plate and may masquerade as a 'chalazion' (Fig. 1.75). It is therefore recommended that any chalazion of an unusual consistency should undergo full-thickness resection and histological examination. Unless treated, the nodule may become very large (Fig. 1.76).
2. **Spreading meibomian gland carcinoma** infiltrates into the dermis and causes a diffuse thickening of the lid margin (Fig. 1.77), similar to a sclerosing BCC, and may also invade the conjunctiva (Fig. 1.78). Pagetoid spread refers to extension of the tumour within the epithelium of the palpebral, forniceal or bulbar conjunctiva (Fig. 1.79). This may lead to the mistaken diagnosis of an inflammatory condition such as 'chronic conjunctivitis', 'superior limbic keratoconjunctivitis' or 'cicatricial pemphigoid'.
3. **Gland of Zeis carcinoma**, which is very rare, is characterized by a discrete, slow-growing, nodular or ulcerative lesion on the lid margin (Fig. 1.80).

Melanoma

Melanoma rarely develops on the eyelids but is potentially lethal. Although pigmentation is a hallmark of skin melanomas, half of lid melanomas are clinically non-pigmented and this may give rise to diagnostic difficulties.

Clinical types

1. **Superficial spreading melanoma** is characterized by a plaque with an irregular outline and variable pigmentation (Fig. 1.81).

Fig. 1.75
Nodular meibomian gland carcinoma (Courtesy of H. Frank)

Fig. 1.76
Very large nodular meibomian gland carcinoma

Fig. 1.77
Spreading meibomian gland carcinoma

Fig. 1.78
Extensive involvement of the lid and adjacent conjunctiva by spreading meibomian gland carcinoma

Fig. 1.79
Involvement of the tarsal conjunctiva by spreading meibomian gland carcinoma (Courtesy of H. Frank)

Fig. 1.80
Ulcerating gland of Zeis carcinoma

2. **Nodular melanoma** is characterized by a blue-black nodule surrounded by normal skin (Fig. 1.82).
3. **Melanoma arising from lentigo maligna.** Lentigo maligna is a slowly expanding pigmented macule which typically affects the elderly and is also referred to as 'Hutchinson freckle'. Occasionally it is associated with the subsequent development of melanoma (Fig. 1.83).

Fig. 1.81
Superficial spreading melanoma

Fig. 1.82
Nodular melanoma

Kaposi sarcoma

Kaposi sarcoma is a vascular tumour which typically affects patients with AIDS. Many patients have advanced systemic disease although in some instances the tumour may be the sole manifestation of AIDS.

1. **Signs.** A small tumour is a pink, red-violet to brown lesion which may be mistaken for a haematoma or a naevus (Fig. 1.84). A large, rapidly growing tumour may ulcerate and bleed (Fig. 1.85).
2. **Treatment** is by radiotherapy or excision.

Merkel cell carcinoma

Merkel cell carcinoma is a fast-growing tumour arising from the dermis which typically affects the elderly. Its rarity may lead to difficulty in diagnosis and delay in treatment of this highly malignant and potentially lethal tumour. In fact, half the patients have metastatic spread at presentation.

Fig. 1.83
Extensive melanoma arising from lentigo maligna

1. **Signs.** A violaceous, well-demarcated nodule with intact overlying skin, most frequently involving the upper eyelid (Fig. 1.86).
2. **Treatment** is by excision which is frequently combined with chemotherapy.

Fig. 1.84
Kaposi sarcoma

Fig. 1.85
Large Kaposi sarcoma

Fig. 1.86
Merkel cell carcinoma (Courtesy of S. Webber)

Principles of treatment

Surgical excision

This should remove the entire tumour but at the same time preserve as much normal tissue as possible. Most small BCC can be cured by excision of the tumour together with a 4 mm margin of tissue which looks clinically normal. More radical surgical excision is required for large BCC and aggressive tumours such as SCC and SGC. Frozen section control by either a standard method or micrographic surgery can further improve the success rate.

1. **Standard frozen section** involves histological examination of the margins of the excised specimen at the time of surgery to ensure that they are tumour-free. If no tumour cells are detected, the eyelid is reconstructed: if some are present in a particular area, further excision is performed until the specimen is tumour-free.
2. **Moh micrographic surgery** involves excision with serial horizontal frozen sections from the undersurface of the tumour. The sections are then colour coded or mapped to identify any remaining areas of tumour. Although time-consuming, this maximizes the chances of total tumour excision with minimal sacrifice of normal tissue. This is a particularly useful technique for tumours that grow diffusely and have indefinite margins with finger-like extensions, such as sclerosing BCC, SGC, recurrent tumours and those involving the medial or lateral canthi.

Technique of reconstruction

This depends on the extent of full-thickness horizontal resection. It is important to reconstruct both anterior and posterior lamellae. If one of the lamellae has been sacrificed during excision of the tumour, it must be reconstructed with similar tissue. The technique depends on the size of the defect and laxity of the lid.

1. **Small defects** involving less than one-third of the eyelid can usually be closed directly, provided the surrounding tissue is sufficiently elastic to allow approximation of the cut edges. If necessary, a lateral cantholysis can be fashioned to mobilize additional tissue if the defect cannot be reapproximated (Fig. 1.87).
2. **Moderate-size defects** involving less than half of the eyelid may require a Tenzel semicircular flap for closure (Fig. 1.88).
3. **Large defects** involving over half of the eyelid may be closed by one of the following techniques:
   a. ***Mustarde cheek rotation flap*** is used for a lower eyelid defect (Fig. 1.89). The posterior lamella is reconstructed with nasal septum cartilage and mucosa or full-thickness buccal mucous membrane or a Hughes flap.
   b. ***Eyelid-sharing procedures*** may also be used, although care should be taken not to compromise upper lid function when reconstructing the lower lid. Figure 1.90 shows reconstruction of the entire lower eyelid following excision of an infiltrating basal cell carcinoma.
   c. ***Glabellar or rhomboid flaps*** may be required for defects involving the medial canthus and medial aspects of the upper eyelid (Fig. 1.91).

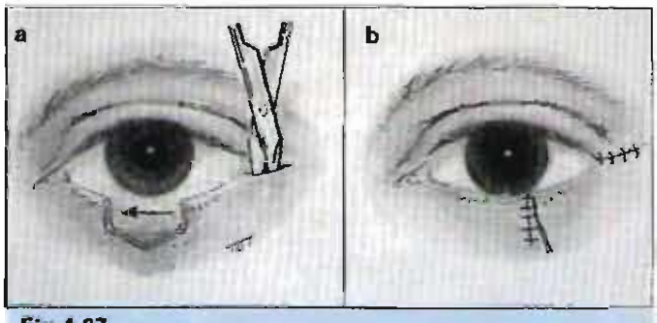

Fig. 1.87
(a) Lateral cantholysis; (b) to enhance closure of a small eyelid defect

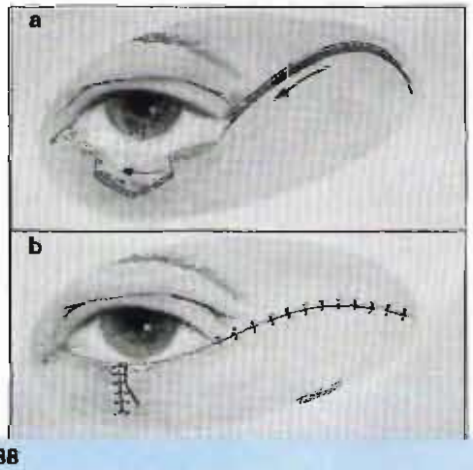

Fig. 1.88
(a) Large lid defect; (b) Tenzel flap

Fig. 1.89
Closure of a large inferior eyelid defect by a Mustarde cheek rotation flap

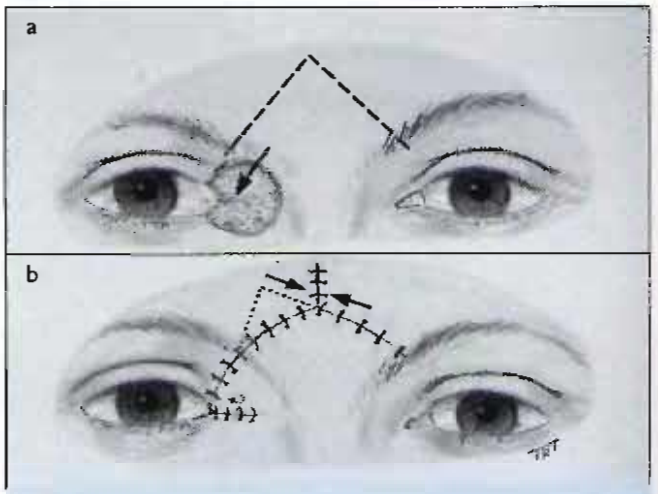

Fig. 1.91
Glabellar flap procedure following excision of a tumour at the medial canthus

Radiotherapy

1. Indications
- Small nodulo-ulcerative BCCs which do not involve the medial canthal area in patients who are either unsuitable for or refuse surgery.
- Kaposi sarcoma because it is radiosensitive.

2. Contraindications
- Medial canthal BCC because radiotherapy would damage the canaliculi and result in epiphora.
- Upper eyelid tumours because subsequent keratinization results in a chronically uncomfortable eye.
- Aggressive tumours such as sclerosing BCC, SCC and SGC.

3. Potential complications
- Skin damage and madarosis (Fig. 1.92).
- Nasolacrimal duct stenosis following irradiation to the medial canthal area.

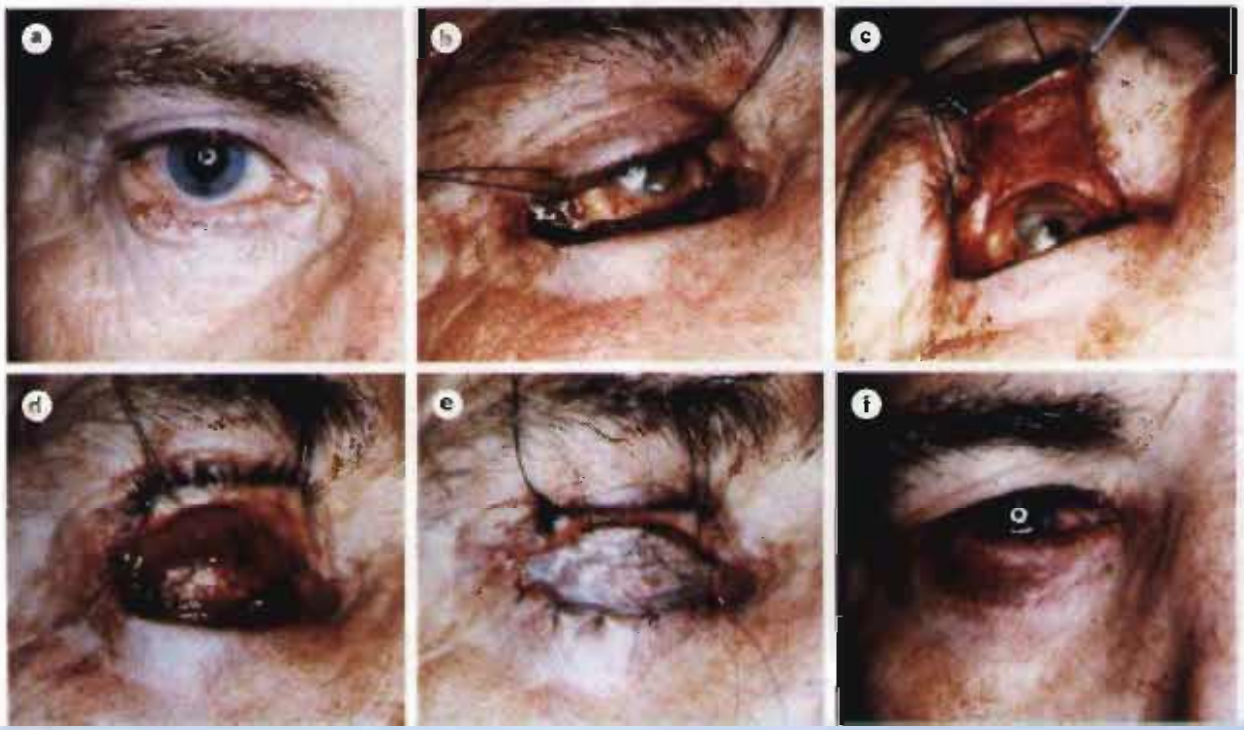

Fig. 1.90
Eyelid-sharing procedure. (a) Preoperative appearance of extensive sclerosing basal cell carcinoma; (b) appearance following total excision; (c and d) fashioning of a tarso-conjunctival flap to fill the defect in the posterior lamella; (e) reconstruction of the anterior lamella with a skin graft; (f) final appearance

Fig. 1.92
Scarring and madarosis induced by radiotherapy for a basal cell carcinoma

- Conjunctival keratinization, dry eye, keratopathy and cataract.
- Retinopathy and optic neuropathy.

NB: Many of these complications can be avoided if the globe is protected by a special eyeshield during irradiation. The recurrence rate is higher than after surgery, and radiotherapy does not allow histological confirmation of tumour eradication. Recurrences following radiotherapy are difficult to treat surgically because of the poor healing properties of irradiated tissue.

Cryotherapy

This does not damage the canalicular system.

1. **Indications.** Small superficial BCC.
2. **Contraindications** are similar to those of radiotherapy, although cryotherapy may be a useful adjunct to surgery in patients with epibulbar pagetoid extensions of SGC, thus sparing the patient an exenteration.
3. **Potential complications** are skin depigmentation, madarosis and conjunctival overgrowth.

Laser microsurgery

This is a relatively new method of treating well-circumscribed BCC of the lid margins without conjunctival extension. The carbon dioxide laser acts as a scalpel to excise the tumour followed by vaporization of the deep and lateral resected margins. The wound is then left to heal by secondary intention.

Ectropion

Involutional ectropion

Involutional (age-related) ectropion affects the lower lid of elderly patients. It results in epiphora and in long-standing cases the tarsal conjunctiva may become chronically inflamed, thickened and keratinized.

Pathogenesis

1. **Horizontal lid laxity** is demonstrated by pulling the central part of the lid 8 mm or more from the globe and its failure to snap back to its normal position on release without the patient first blinking (Fig. 1.93).
2. **Medial canthal tendon laxity** is demonstrated by pulling the lower lid laterally and observing the position of the inferior punctum (Fig. 1.94a). If the lid is normal the punctum should not be displaced more than 1–2 mm. If laxity is mild the punctum reaches the limbus, and if severe it reaches the pupil.
3. **Lateral canthal tendon laxity** is characterized by a rounded appearance of the lateral canthus and the ability to pull the lower lid medially more than 2 mm (Fig. 1.94b).

Treatment

The chosen method depends on the following: (a) extent of ectropion (i.e. predominantly medial or generalized), (b) extent of horizontal lid laxity, (c) severity of canthal tendon laxity and (d) degree of excess skin.

1. **Medial ectropion** (Fig. 1.95a) is treated by the Lazy-T procedure, which involves excision of a tarsoconjunctival diamond (medial spindle) about 4 mm high and 8 mm long, parallel with and inferior to the canaliculus and punctum, together with excision of a pentagon of full-thickness lid lateral to the punctum (Fig. 1.95b).
2. **Generalized ectropion** (Fig. 1.96a) is treated by horizontal lid shortening in which a pentagon of full-thickness lid is excised where the ectropion is most marked (Fig. 1.96b). Significant medial canthal tendon laxity should also be corrected.
3. **Marked generalized ectropion with excess skin** (Fig. 1.97a) is treated with the Kuhnt–Szymanowski procedure, in which a pentagon of full-thickness lid is excised laterally together with a lateral triangle of redundant skin (Fig. 1.97b). Significant medial canthal tendon laxity should also be corrected.

Fig. 1.93
Involutional ectropion

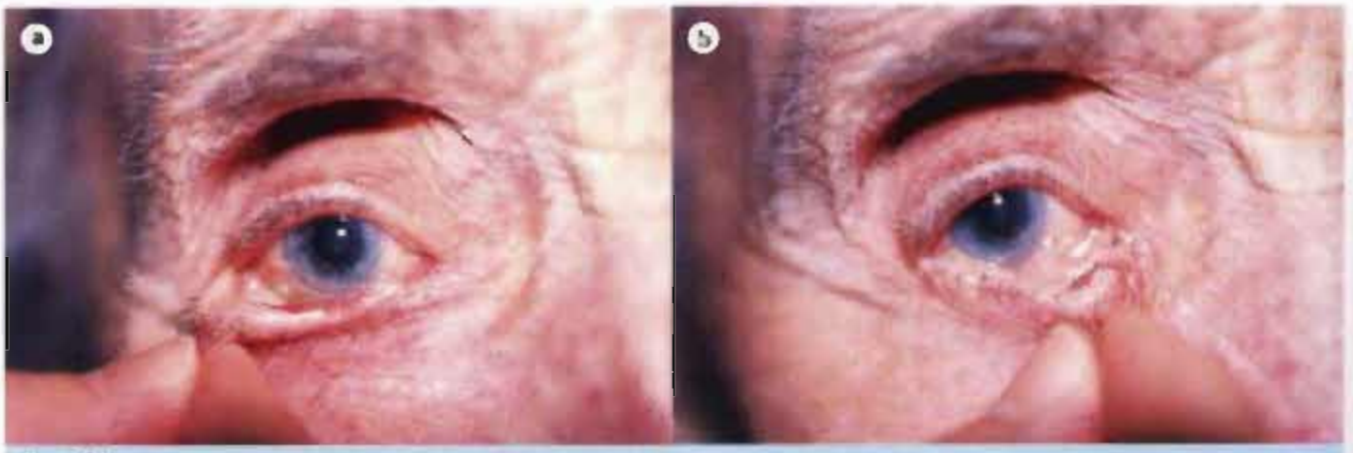

Fig. 1.94
Involutional ectropion. (a) Medial canthal tendon laxity; (b) lateral canthal tendon laxity

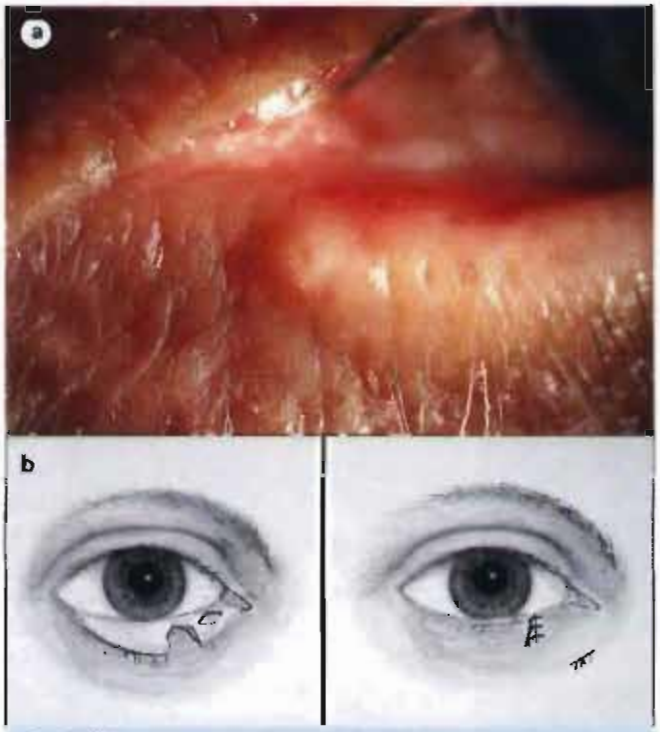

Fig. 1.95
(a) Medial ectropion; (b) lazy-T procedure

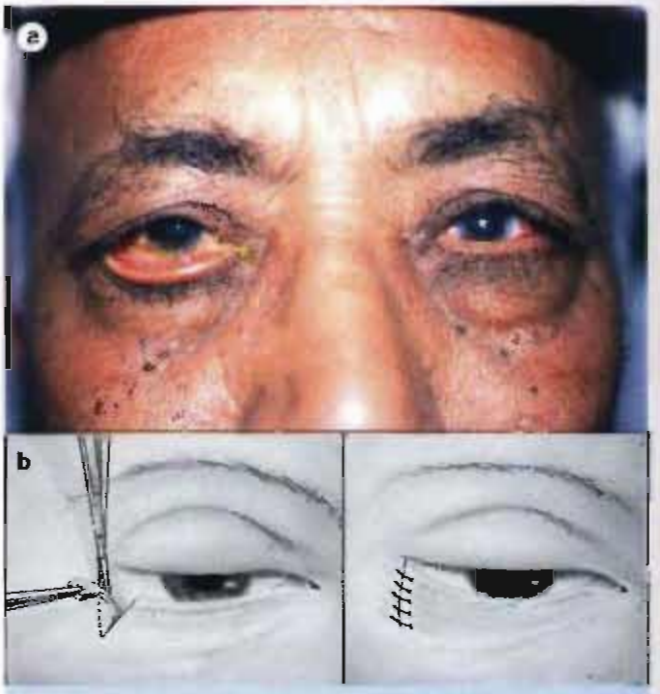

Fig. 1.96
(a) Generalized ectropion without excess skin; (b) horizontal lid shortening

Cicatricial ectropion

Cicatricial ectropion is caused by scarring or contracture of the skin and underlying tissues which pulls the eyelid away from the globe (Fig. 1.98). If the skin is pushed over the orbital margin with a finger the ectropion will be relieved and the lids will close. Opening the mouth tends to accentuate the ectropion. Depending on the cause, both lids may be involved and the defect may be local (e.g. trauma) or general (e.g. burns, dermatitis, ichthyosis).

1. **Mild localized** cases are treated by excision of the offending scar tissue combined with a procedure that lengthens vertical skin deficiency such as 'Z'-plasty (Fig. 1.99).
2. **Severe generalized** cases require transposition flaps or free skin grafts. Sources of skin include upper lids, as well as posterior auricular, preauricular and supraclavicular areas.

Paralytic ectropion

Paralytic ectropion is caused by an ipsilateral facial nerve palsy and is associated with retraction of the upper and lower lids and brow ptosis. The latter may cause narrowing of the palpebral aperture.

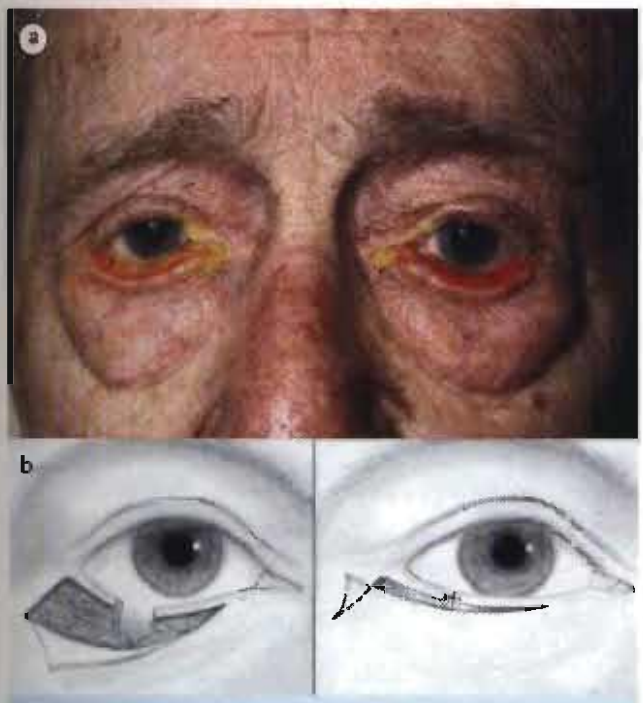

Fig. 1.97
(a) Generalized ectropion with excess skin;
(b) Kuhnt–Szymanowski procedure

Fig. 1.98
Cicatricial ectropion due to trauma

Potential complications

1. **Exposure keratopathy** is caused by a combination of lagophthalmos (Fig. 1.100) and inadequate resurfacing of the tear film over the cornea by the lids.
2. **Epiphora** is caused by malposition of the inferior lacrimal punctum, failure of the lacrimal pump mechanism and an increase in tear production resulting from corneal exposure.

Temporary treatment

This is aimed at protecting the cornea in anticipation of spontaneous recovery of facial nerve function.

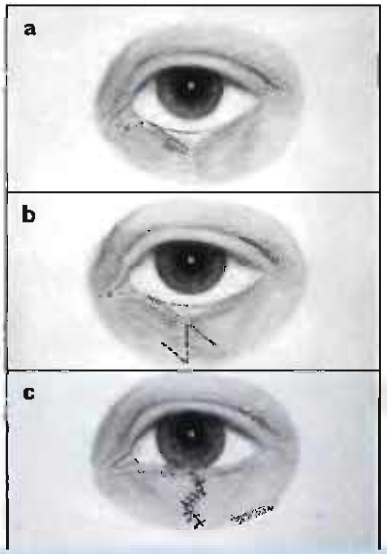

Fig. 1.99
Vertical lid-lengthening ('Z'-plasty)

Fig. 1.100
Bilateral paralytic ectropion and lagophthalmos due to facial nerve palsies

1. **Lubrication** with tear substitutes during the day and instillation of ointment and taping shut of the lids during sleep are usually adequate in mild cases.
2. **Temporary tarsorrhaphy**, a procedure in which the lateral aspect of the upper and lower lids are sutured together (Fig. 1.101), may be necessary in patients with a poor Bell phenomenon, in which the cornea remains exposed when the patient attempts to blink.

Permanent treatment

This should be considered when there has been no improvement of a Bell palsy after 3 months or when there is permanent damage to the facial nerve, as may occur following removal of an acoustic neuroma. Treatment is aimed at reducing horizontal and vertical dimensions of the palpebral aperture by one of the following procedures:

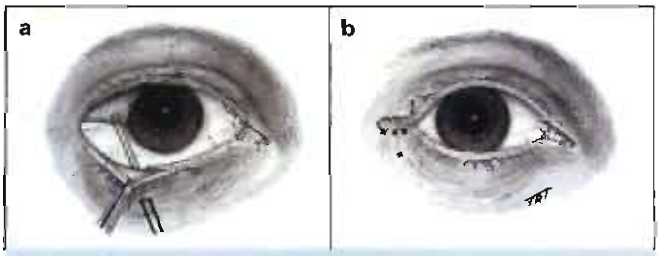

Fig. 1.101
Lateral tarsorrhaphy

Fig. 1.102
Mechanical ectropion due to a tumour

1. **Medial canthoplasty** may be performed if the medial canthal tendon is intact. The eyelids are sutured together medial to the lacrimal puncta so that the puncta become inverted and the fissure between the inner canthus and puncta is shortened.
2. **Medial wedge resection** with attachment of tarsus to the posterior lacrimal crest is used to correct medial ectropion associated with medial canthal laxity.
3. **Lateral canthal sling** may be used to correct residual ectropion and raise the lateral canthus.

Mechanical ectropion

Mechanical ectropion is caused by tumours on or near the lid margin which mechanically evert the lid (Fig. 1.102). Treatment involves removal of the cause, if possible, and correction of significant horizontal lid laxity.

Entropion

Involutional entropion

Involutional (age-related) entropion affects mainly the lower lid because the upper has a broader tarsus and is more stable.

The constant rubbing of the lashes on the cornea in patients with long-standing entropion (pseudo-trichiasis) may cause irritation, corneal punctate epithelial erosions and, in severe cases, ulceration and pannus formation (Fig. 1.103).

Pathogenesis

This involves age-related degeneration of elastic and fibrous tissues within the eyelid resulting in the following (Fig. 1.104):

1. **Horizontal lid laxity** caused by stretching of the canthal tendons and tarsal plate.
2. **Vertical lid instability** caused by attenuation, dehiscence or disinsertion of the lower lid retractors. Weakness of the latter is recognized by decreased excursion of the lower lid in downgaze.
3. **Over-riding** of the pretarsal by the preseptal orbicularis during lid closure tends to move the lower border of the tarsus anteriorly, away from the globe, and the upper border towards the globe, thus tipping the lid inwards.

Fig. 1.103
Corneal ulceration due to pseudo-trichiasis associated with involutional entropion

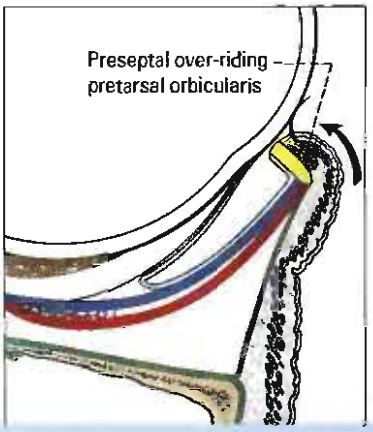

Fig. 1.104
Pathogenesis of involutional entropion

Treatment

Temporary treatment is with lubricants, taping, orbicularis chemodenervation with botulinum toxin injection or soft bandage contact lenses. Surgical treatment is determined principally by the severity of horizontal lid laxity.

1. **Horizontal lid laxity absent**
   - *a. Transverse everting sutures* prevent over-riding of the preseptal orbicularis and provide temporary correction lasting several months (Fig. 1.105).
   - *b. Weis procedure* gives a lasting correction (Fig. 1.106). It consists of full-thickness horizontal lid-splitting and insertion of everting sutures. The scar creates a barrier between the preseptal and pretarsal orbicularis, and the everting suture transfers the pull of the lower lid retractors from the tarsus to the skin and orbicularis.
   - *c. Jones procedure* can be performed as primary treatment but is frequently reserved for recurrences. It tightens the lower lid retractors, thus increasing their pull, and creates a barrier between the preseptal and pretarsal orbicularis (Fig. 1.107).
2. **Horizontal lid laxity present**. This requires transverse lid splitting, inserting of everting sutures and horizontal lid shortening (Quickert procedure). Significant canthal tendon laxity should also be corrected.

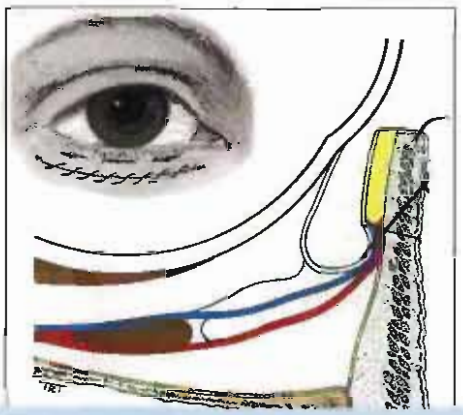

Fig. 1.106
Weis procedure

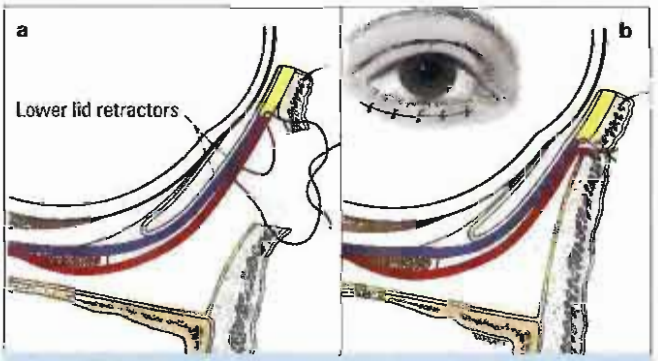

Fig. 1.107
Jones procedure

Cicatricial entropion

Cicatricial entropion is caused by severe scarring of the palpebral conjunctiva, which pulls the upper or lower lid margin towards the globe (Fig. 1.108). Causes include cicatrizing conjunctivitis, trachoma, trauma and chemical injuries.

1. **Medical** treatment is aimed at keeping the lashes away from the cornea by bandage contact lenses.
2. **Surgical** treatment of mild cases is by transverse tarsotomy (tarsal fracture) with anterior rotation of the lid margin. Treatment of severe cases is difficult and is directed at replacing deficient or keratinized conjunctiva and replacing the scarred and contracted tarsus with composite grafts.

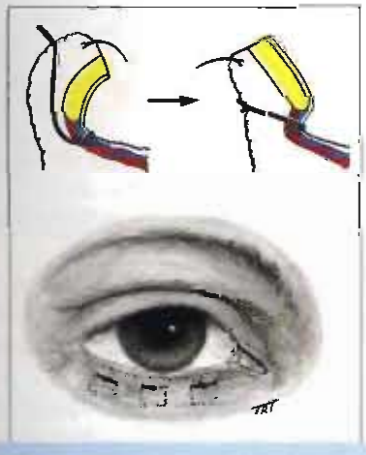

Fig. 1.105
Transverse lid-everting sutures

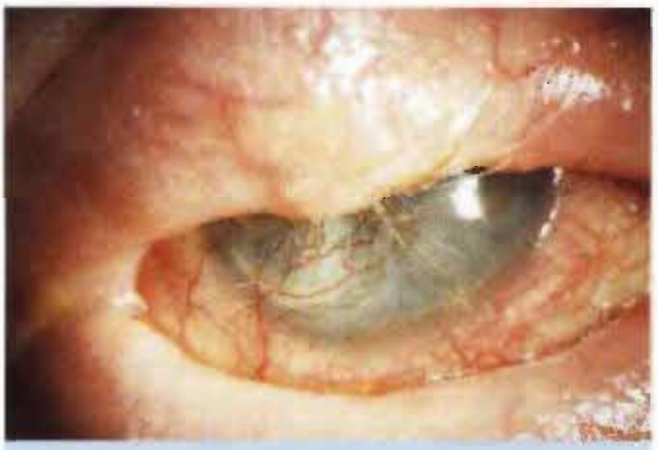

Fig. 1.108
Cicatricial upper lid entropion resulting in corneal scarring and vascularization

Fig. 1.109
Congenital lower lid entropion

Congenital entropion

Upper lid entropion

This is usually secondary to mechanical effects of microphthalmos which cause variable degrees of upper lid inversion.

Lower lid entropion

This is caused by improper development of the inferior retractor aponeurosis.

1. **Signs**. Inturning of the entire lower eyelid and lashes with absence of the lower lid crease (Fig. 1.109), which should not be confused with epiblepharon.
2. **Treatment** involves the excision of a strip of skin and muscle, and fixation of the skin crease to the tarsal plate (Hotz procedure).

Ptosis

Classification

Ptosis is an abnormally low position of the upper lid which may be congenital or acquired. An anatomical classification is shown in Table 1.4.

1. **Neurogenic ptosis** is caused by an innervational defect such as third nerve and oculosympathetic palsy (*see* Chapter 18).
2. **Myogenic ptosis** is caused by a myopathy of the levator muscle itself, or by impairment of transmission of impulses at the neuromuscular junction (neuromyopathic). Acquired myogenic ptosis occurs in myasthenia gravis, myotonic dystrophy (*see* Chapter 20) and ocular myopathies (*see* Chapter 18).

Table 1.4 Classification of ptosis

1. **Neurogenic**
   - third nerve palsy
   - Horner syndrome
   - Marcus Gunn jaw-winking syndrome
   - third nerve misdirection
2. **Myogenic**
   - myasthenia gravis
   - myotonic dystrophy
   - ocular myopathy
   - simple congenital
   - blepharophimosis syndrome
3. **Aponeurotic**
   - involutional
   - postoperative
4. **Mechanical**
   - dermatochalasis
   - tumours
   - oedema
   - anterior orbital lesions
   - scarring

3. **Aponeurotic** ptosis is caused by a defect in the levator aponeurosis.
4. **Mechanical** ptosis is caused by gravitational effect of a mass or scarring.

Clinical evaluation

History

The age at onset of ptosis and its duration will usually distinguish congenital from acquired cases. If the history is ambiguous, old photographs may be helpful. It is also important to enquire about symptoms of possible underlying systemic disease, such as associated diplopia, variability of ptosis during the day and excessive fatigue.

Pseudoptosis

This false impression of ptosis may be caused by the following:

1. **Lack of support** of the lids by the globe may be due to an orbital volume deficit associated with an artificial eye, microphthalmos, phthisis bulbi or enophthalmos (Fig. 1.110).
2. **Contralateral lid retraction**, which is detected by comparing the levels of the upper lids, remembering that the margin of the upper lid normally covers the superior 2 mm of the cornea (Fig. 1.111).
3. **Ipsilateral hypotropia**, because the upper lid follows the globe downwards (Fig. 1.112). The pseudoptosis will disappear when the hypotropic eye assumes fixation on covering the normal eye.

Fig. 1.110
Right pseudoptosis due to an artificial eye

Fig. 1.113
Brow ptosis

Fig. 1.111
Left pseudoptosis due to retraction of the right upper lid

Fig. 1.114
Pseudoptosis due to dermatochalasis

Fig. 1.112
Left pseudoptosis due to ipsilateral hypotropia

4. **Brow ptosis** due to excessive skin on the brow or seventh nerve palsy which is diagnosed by manually elevating the eyebrow (Fig. 1.113).
5. **Dermatochalasis** in which excessive skin on the upper lids may cause both a pseudo- and a real ptosis (Fig. 1.114).

Measurements

1. **Margin–reflex distance** is the distance between the upper lid margin and the corneal reflection of a pen torch held by the examiner, at which the patient is directly looking (Fig. 1.115). The normal is 4–4.5 mm.
2. **Vertical fissure height** is the distance between the upper and lower lid margins, measured in the pupillary plane (Fig. 1.116). The upper lid margin normally rests about 2 mm below the upper limbus and the lower 1 mm above the lower limbus. This measurement is less in males (7–10 mm) than in females (8–12 mm). Unilateral ptosis can be quantified by comparison with the contralateral side. Ptosis may be graded as mild (up to 2 mm), moderate (3 mm) and severe (4 mm or more).
3. **Levator function** (upper lid excursion) is measured by placing a thumb firmly against the patient's brow to negate the action of the frontalis muscle, with the eyes in downgaze (Fig. 1.117a). The patient then looks up as far as possible and the amount of excursion is measured with a rule (Fig. 1.117b). Levator function is graded as normal (15 mm or more), good (12–14 mm), fair (5–11 mm) and poor (4 mm or less).

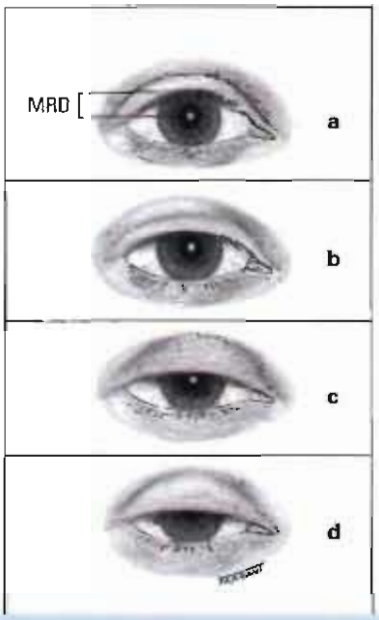

Fig. 1.115
Margin–reflex distance. (a) Normal; (b) mild ptosis; (c) moderate ptosis; (d) severe ptosis

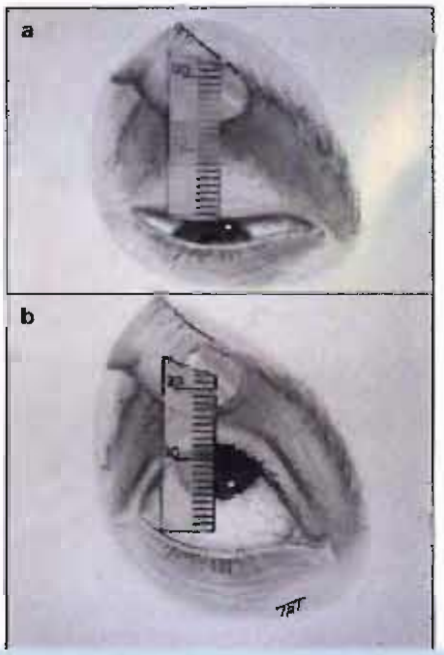

Fig. 1.117
Measurement of levator function

Fig. 1.116
Measurement of vertical fissure height

Fig. 1.118
Upper lid crease

4. **Upper lid crease** is the vertical distance between the lid margin and the lid crease in downgaze (Fig. 1.118). In females it measures about 10 mm and in males 8 mm. Absence of the crease in a patient with congenital ptosis is indirect evidence of poor levator function, whereas a high crease suggests an aponeurotic defect. The skin crease is also used as a guide to the initial incision.
5. **Pretarsal show** is the distance between the lid margin and the skin fold with the eyes in the primary position.

Associated signs

1. **Increased innervation** may flow to the levator muscle of a unilateral ptosis, particularly in upgaze. Associated increased innervation to the contralateral normal levator will result in lid retraction (Fig. 1.119). The examiner should therefore manually elevate the ptotic lid and look for a droop of the opposite lid. If this occurs, the patient

Fig. 1.119
Left ptosis resulting in right lid retraction

should be warned that surgical correction may induce a drop in the opposite lid.

2. **Fatiguability** is tested by asking the patient to look up without blinking for 30 seconds. Progressive drooping of one or both lids, or inability to maintain upgaze, is suggestive of myasthenia (Fig. 1.120). Myasthenic ptosis may show an overshoot of the upper lid on saccade from downgaze to the primary position (Cogan twitch sign) and also a 'hop' on sidegaze.
3. **Ocular motility defects**, particularly of the superior rectus, must be evaluated in patients with congenital ptosis. Correction of an ipsilateral hypotropia may improve the degree of ptosis.
4. **Jaw-winking** phenomenon can be detected by asking the patient to chew and move the jaws from side to side (*see* below).
5. **Bell phenomenon** is tested by manually holding the lids open, asking the patient to try to close the eyes and observing upward rotation of the globe. A weak Bell phenomenon carries a risk of postoperative exposure keratopathy, particularly following large levator resections or suspension procedures.

Fig. 1.120
Increase in ptosis on fatigue testing

Marcus Gunn jaw-winking syndrome

About 5% of all cases of congenital ptosis manifest the Marcus Gunn jaw-winking phenomenon. The vast majority of cases are unilateral. Although the exact aetiology is unclear, it has been postulated that a branch of the mandibular division of the fifth cranial nerve is misdirected to the levator muscle.

Signs

- Retraction of the ptotic lid in conjunction with stimulation of the ipsilateral pterygoid muscles by chewing, sucking, opening the mouth (Fig. 1.121) or contralateral jaw movement (Fig. 1.122).
- Less common stimuli to winking include jaw protrusion, smiling, swallowing and clenching of teeth.
- Jaw-winking does not improve with age, although patients may learn to mask it.

Treatment

This should be considered if jaw-winking or ptosis represents a significant functional or cosmetic problem. Although no surgical treatment is entirely satisfactory, possible approaches include:

1. **Unilateral levator resection** for mild cases with levator function 5 mm or better.
2. **Unilateral levator disinsertion** and part resection with ipsilateral brow (frontalis) suspension for more severe cases.
3. **Bilateral levator disinsertion** and part resection with bilateral brow suspension to produce a symmetrical result.

Fig. 1.121
Marcus Gunn jaw-winking syndrome. **(a)** Normal position showing a moderate left ptosis; **(b)** retraction of left eyelid on opening the mouth

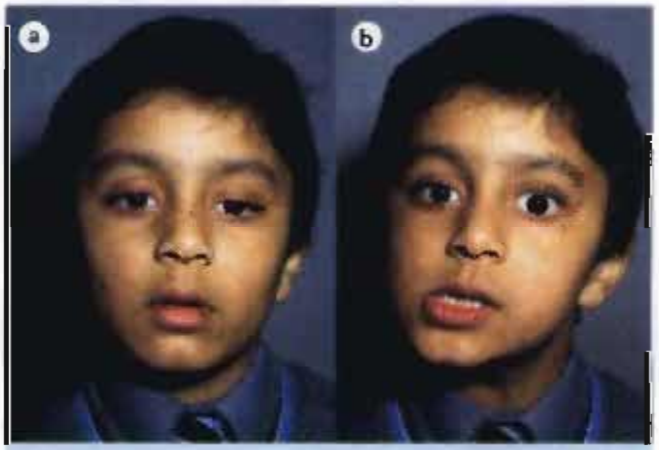

Fig. 1.122
Marcus Gunn jaw-winking syndrome. **(a)** Normal position showing a mild left ptosis; **(b)** retraction of the left eyelid on moving the jaw to the contralateral side

Third nerve misdirection

Third nerve misdirection syndromes may be congenital or, more frequently, follow acquired third nerve palsies.

1. **Signs**. Bizarre movements of the upper lid which accompany various eye movements (Fig. 1.123).
2. **Treatment** is by levator disinsertion and brow suspension.

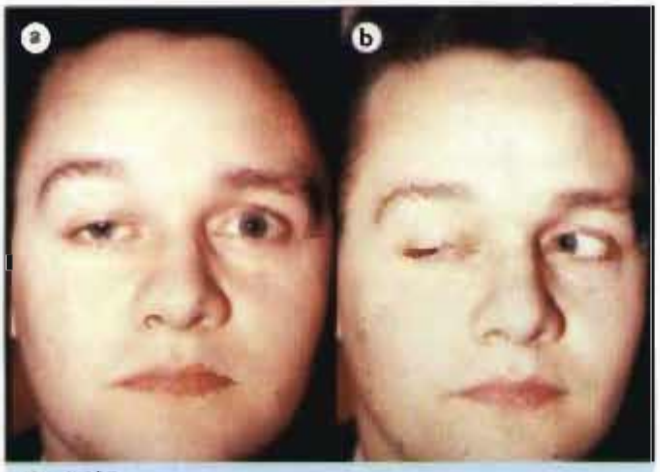

Fig. 1.123
Third nerve misdirection. (a) Normal position showing a moderate right ptosis; (b) worsening of ptosis on right gaze
(Courtesy of S.Vardy)

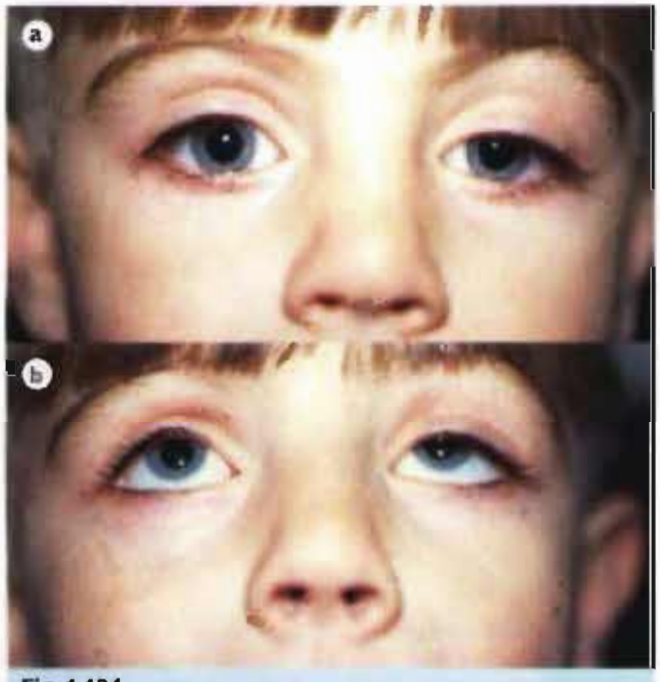

Fig. 1.124
(a) Moderate left congenital ptosis with absent lid crease; (b) poor levator function

Simple congenital ptosis

Simple congenital ptosis is probably caused by failure of neuronal migration or development with muscular sequelae. A minority of cases are hereditary.

Signs

- Unilateral or bilateral ptosis of variable severity.
- Absent upper lid crease and poor levator function (Fig. 1.124).
- In downgaze the ptotic lid is higher than the normal because of poor relaxation of the levator muscle. This is in contrast to acquired ptosis in which the affected lid is level with or lower than the normal on downgaze.

> ***NB:*** Following surgical correction the lid lag in downgaze may worsen (Fig. 1.125).

Associations

- Superior rectus weakness may be present because of its close embryological association with the levator.
- Compensatory chin elevation in severe bilateral cases (Fig. 1.126).
- Refractive errors are common and more frequently responsible for amblyopia than the ptosis itself.

Treatment

This should be carried out during the preschool years when accurate measurements can be obtained, although it may be considered earlier in severe cases to prevent amblyopia. Most cases require levator resection.

Blepharophimosis syndrome

The blepharophimosis syndrome is a rare, autosomal dominant, congenital disorder.

Fig. 1.125
Left lid is higher than the right following surgery for congenital ptosis

Fig. 1.126
Compensatory chin elevation for severe bilateral congenital ptosis

Fig. 1.127
Blepharophimosis syndrome

1. **Signs** (Fig. 1.127)
   - Moderate to severe symmetrical ptosis with poor levator function.
   - Short horizontal palpebral aperture.
   - Telecanthus and epicanthus inversus.
   - Lateral ectropion of lower lids.
   - Poorly developed nasal bridge and hypoplasia of the superior orbital rims.
2. **Treatment** initially involves correction of epicanthus and telecanthus followed a few months later by bilateral frontalis suspension. It is also important to treat amblyopia, which is present in about 50% of cases.

Aponeurotic ptosis

Aponeurotic ptosis is caused by dehiscence, disinsertion or stretching of the levator aponeurosis which restricts transmission of force from a normal levator muscle to the upper lid. It is most frequently caused by involutional age-related degenerative changes.

1. **Signs** (Fig. 1.128)
   - Variable, usually bilateral ptosis with good levator function.
   - High upper lid crease (12 mm or more) because the posterior attachments of the aponeurosis to the tarsus have detached whereas the anterior attachments to the skin have remained intact and pulled the skin crease superiorly.
   - In severe cases the upper lid crease may be absent, the eyelid above the tarsal plate very thin and the upper sulcus deep (Fig. 1.129).

Fig. 1.128
(a) Moderate right involutional ptosis with brow over-action; (b) high right upper lid crease as compared to left; (c) good levator function

Fig. 1.129
Severe bilateral involutional ptosis with thinning of the lids above the tarsal plates and deep sulci

Fig. 1.130
Mechanical ptosis due to a neurofibroma

NB: Involutional ptosis may be confused with myasthenic ptosis because it frequently gets worse towards the end of the day. This is because of fatigue of the Müller muscle, which has to work harder to keep the lid elevated.

2. **Treatment** options include levator resection, reinsertion or anterior levator aponeurosis repair.

Mechanical ptosis

Mechanical ptosis is the result of impaired mobility of the upper lid. It may be caused by dermatochalasis, large eyelid tumours such as neurofibromas (Fig. 1.130), scarring, severe lid oedema and anterior orbital lesions.

Principles of surgery

Fasanella–Servat procedure

1. **Indications**. Mild ptosis with levator function of at least 10 mm. This includes most cases of Horner syndrome and very mild congenital ptosis.

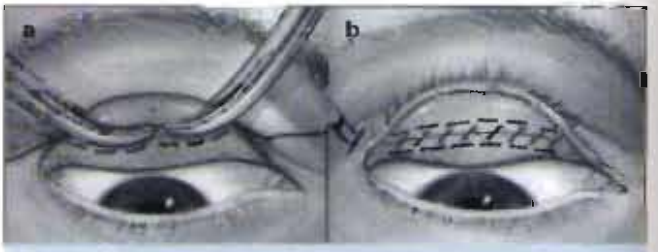

Fig. 1.131
Fasanella–Servat procedure

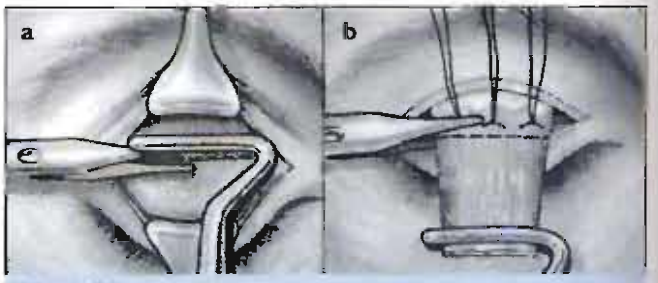

Fig. 1.132
Levator resection

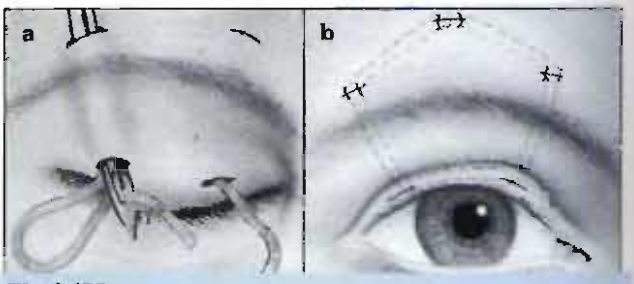

Fig. 1.133
Frontalis suspension

2. **Technique**. The upper border of the tarsus is excised together with the lower border of Müller muscle and overlying conjunctiva (Fig. 1.131).

Levator resection

1. **Indications**. Any ptosis, provided levator function is at least 5 mm. The amount of resection is determined by levator function and the severity of ptosis.
2. **Technique**. Shortening of the levator complex through an anterior (skin) or posterior (conjunctival) approach (Fig. 1.132).

Frontalis suspension

1. **Indications**
   - Severe ptosis (>4 mm) with very poor levator function (<4 mm).
   - Marcus Gunn jaw-winking syndrome.
   - Aberrant regeneration of the third nerve.

- Blepharophimosis syndrome.
- Total third nerve palsy.
- Unsatisfactory result from a previous levator resection.

2. **Technique.** Suspension of the tarsus from the frontalis muscle with a sling consisting of autologous fascia lata or non-absorbable synthetic material such as proline or silicone (Fig. 1.133).

Aponeurosis repair

1. **Indications.** Aponeurotic ptosis with excellent levator function.
2. **Technique.** Advancement and suturing of healthy aponeurosis to the tarsal plate through an anterior or posterior approach.

Miscellaneous acquired disorders

Dermatochalasis

Dermatochalasis is a very common, usually bilateral condition which typically affects elderly patients, characterized by redundant upper lid skin which may be associated with herniation of fat through a weak orbital septum (Fig. 1.134). The lids have a baggy appearance with indistinct lid creases (*see* Fig. 1.114). Treatment of severe cases, involves excision of redundant skin (blepharoplasty).

Blepharochalasis

Blepharochalasis is a rare condition characterized by recurrent episodes of painless, non-pitting oedema of both upper lids which usually resolves spontaneously after a few days. It usually starts around puberty and, with time, the episodes become less frequent. Severe cases may cause stretching of upper lid skin so that it becomes redundant and may acquire the appearance of wrinkled cigarette paper (Fig. 1.135). In other cases weakening of the orbital septum results in fat herniation.

Fig. 1.134
Fat herniation in dermatochalasis

Fig. 1.135
Left aponeurotic ptosis and very thin upper lid skin resulting from blepharochalasis

Floppy eyelid syndrome

Floppy eyelid syndrome is an uncommon, unilateral or bilateral condition, which is frequently misdiagnosed. It

Fig. 1.136
Floppy eyelid syndrome. (a) Loose upper eyelids; (b) severe conjunctivitis of exposed areas

typically affects very obese men who may also suffer from sleep apnoea and snoring.

1. **Signs**
   - Rubbery and loose upper eyelids (Fig. 1.136a).
   - Eversion of the lids during sleep results in trauma to the exposed tarsal conjunctiva and chronic papillary conjunctivitis (Fig. 1.136b).
2. **Treatment** of mild cases involves nocturnal eye shields or taping of the lids. Severe cases require horizontal lid shortening.

Lid retraction

Lid retraction is suspected when the upper lid margin is either level with or above the superior limbus (Fig. 1.137). The classification is shown in Table 1.5.

Fig. 1.137
Bilateral lid retraction in thyrotoxicosis

Table 1.5 Causes of lid retraction

1. **Thyroid eye disease**
2. **Neurogenic**
   - contralateral unilateral ptosis
   - facial palsy due to unopposed levator action
   - third nerve misdirection
   - Marcus Gunn jaw-winking syndrome
   - Collier sign of the midbrain (Parinaud syndrome)
   - hydrocephalus
   - sympathomimetic drops
3. **Mechanical**
   - surgical overcorrection of ptosis
   - scarring of upper lid skin
4. **Congenital**
   - isolated
   - Duane retraction syndrome
   - Down syndrome
   - transient 'eye popping' reflex in normal infants
5. **Miscellaneous**
   - prominent globe (pseudo-lid retraction)
   - uraemia (Summerskill sign)

Miscellaneous congenital disorders

Epicanthic folds

Epicanthic folds are bilateral vertical folds of skin that extend from the upper or lower lid towards the medial canthus. They may give rise to a pseudo-esotropia.

1. **Signs**
   - *a. **Palpebralis***. The folds are symmetrically distributed between the upper and lower lid (Fig. 1.138). This is the most common type in Caucasians.
   - *b. **Tarsalis***. The folds originate in the medial aspect of the upper lid and extend medially before dissipating (Fig. 1.139). This is the most common type in Orientals.
   - *c. **Inversus***. The folds start in the lower lid and extend upwards to the medial canthal area. It is associated with the blepharophimosis syndrome (*see* Fig. 1.127).

Fig. 1.138
Epicanthus palpebralis and pseudo-esotropia

Fig. 1.139
Epicanthus tarsalis

d. Superciliaris. The folds arise above the brow and extend downwards to the lateral aspect of the nose.

2. **Treatment** of small folds is by Y-V plasty, whilst large folds require a Mustarde Z-plasty.

Telecanthus

Telecanthus is an uncommon condition characterized by increased distance between the medial canthi as a result of abnormally long medial canthal tendons (Fig. 1.140). It should not be confused with hypertelorism, in which there is wide separation of the orbits. Telecanthus may occur in isolation or it may be associated with the blepharophimosis syndrome.

1. **Systemic associations** include Waardenburg, Möbius, Treacher Collins, Rubinstein–Taybi and Turner syndromes.
2. **Treatment** is by shortening and refixation of the medial canthal tendons to the anterior lacrimal crests or a transnasal wire.

Epiblepharon

Epiblepharon is very common in Orientals and should not be confused with the much less common congenital entropion.

1. **Signs.** An extra horizontal fold of skin stretches across the anterior lid margin and the lashes are directed vertically, especially in the medial part of the lid (Fig. 1.141a). When the fold of skin is pulled down the lashes turn out and the normal location of the lid becomes apparent (Fig. 1.141b). In congenital entropion, however, the entire eyelid becomes pulled away from the globe.
2. **Treatment** is not required in the majority of cases because spontaneous resolution with age is the rule. Persistent cases are treated by excising a strip of skin and muscle, and fixation of the skin crease to the tarsal plate (Hotz procedure).

Fig. 1.140
Telecanthus

Fig. 1.142
Coloboma of the upper lid

Fig. 1.141
(a) Epiblepharon; (b) normal position following manual correction

Fig. 1.143
Lower lid colobomas in Treacher Collins syndrome

Coloboma

A coloboma is an uncommon, congenital, unilateral or bilateral, partial or full-thickness eyelid defect.

1. **Upper lid** colobomas occur at the junction of the inner and middle thirds and are not associated with systemic anomalies (Fig. 1.142).
2. **Lower lid** colobomas occur at the junction of the middle and outer thirds and are frequently associated with systemic conditions such as Treacher Collins syndrome (Fig. 1.143).
3. **Treatment** of small to moderate defects is by primary closure, while large defects require skin grafts and rotation flaps.

CHAPTER 2

Lacrimal Drainage System

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Introduction

Applied anatomy

The lacrimal drainage system consists of the following structures (Fig. 2.1):

1. **The puncta** are located at the posterior edge of the lid margin, at the junction of the lash-bearing lateral five-sixths (pars ciliaris) and the non-ciliated medial one-sixth (pars lacrimalis) of each lid. Normally they face slightly posteriorly and can be inspected by everting the medial aspect of the lids. Treatment of excessive watering caused by punctal stenosis or malposition is relatively straightforward.
2. **The canaliculi** pass vertically from the lid margin (the ampullae) for about 2 mm. They then turn medially and run horizontally for about 8 mm to reach the lacrimal sac. The superior and inferior canaliculi most often unite to form the common canaliculus, which opens into the lateral wall of the lacrimal sac. In some individuals, each canaliculus opens separately. A small flap of mucosa (valve of Rosenmuller) overhangs the junction of the common canaliculus and the lacrimal sac and prevents reflux of tears into the canaliculi. Treatment of canalicular obstruction is frequently complicated.
3. **The lacrimal sac** is about 10 mm long and lies in the lacrimal fossa between the anterior and posterior lacrimal crests. The lacrimal bone and the frontal process of the maxilla separate the lacrimal sac from the middle meatus of the nasal cavity. In a dacryocystorhinostomy (DCR) an anastomosis is created between the sac and the nasal mucosa to bypass an obstruction in the nasolacrimal duct.
4. **The nasolacrimal duct** is about 12 mm long and is the inferior continuation of the lacrimal sac. It descends and angles slightly laterally and posteriorly to open into the inferior nasal meatus, lateral to and below the inferior turbinate. The opening of the duct is partially covered by a mucosal fold (valve of Hasner). Obstruction of the duct may cause a secondary distension of the sac.

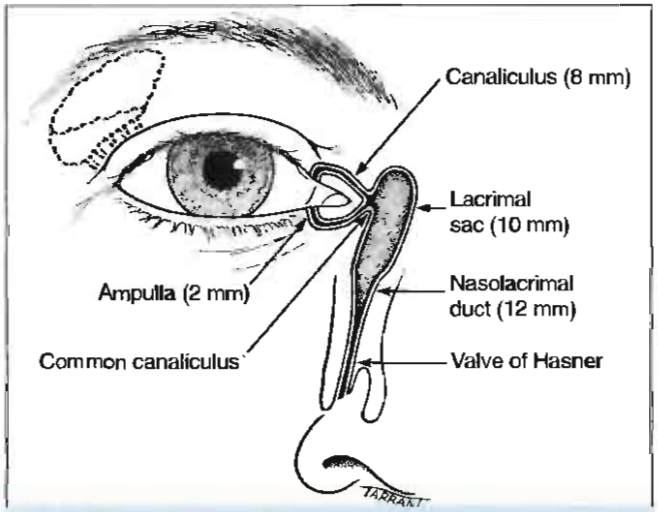

Fig. 2.1
Anatomy of the lacrimal drainage system

Applied physiology

Tears secreted by the main and accessory lacrimal glands pass laterally across the ocular surface. A variable amount of the aqueous component of the tear film is lost by evaporation. This is related to the size of the palpebral aperture, the blink rate, ambient temperature and humidity. The remainder of the tears drain as follows (Fig. 2.2):

1. Tears flow along the upper and lower marginal strips and enter the upper and lower canaliculi by capillarity and also possibly by suction. About 70% of tears drain through the lower canaliculus and the remainder through the upper (Fig. 2.2a).
2. With each blink, the pretarsal orbicularis oculi compresses the ampullae, shortens the horizontal canaliculi and moves the puncta medially (Fig. 2.2b). Simultaneously, the lacrimal part of the orbicularis oculi, which is attached to the fascia of the lacrimal sac, contracts and expands the sac, thereby creating a negative pressure which sucks the tears from the canaliculi into the sac.
3. When the eyes open the muscles relax, the sac collapses and a positive pressure is created which forces the tears

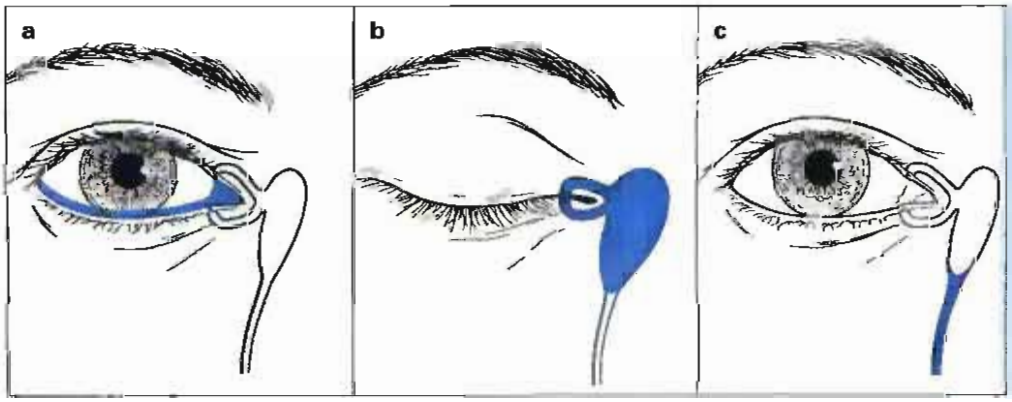

Fig. 2.2
Physiology of the lacrimal pump mechanism

down the nasolacrimal duct into the nose (Fig. 2.2c). Gravity also plays a role. The puncta move laterally, the canaliculi lengthen and fill with tears.

Causes of watering

Overflow of tears may represent lacrimation or epiphora.

1. **Lacrimation** (hyperlacrimation) is caused by reflex lacrimal hypersecretion secondary to ocular inflammation or surface disease. In these cases watering is associated with symptoms of the underlying cause and treatment is usually medical.
2. **Epiphora** is due to compromise of lacrimal drainage. It is exacerbated by a cold and windy atmosphere, and is least in a warm dry room. It may be caused by:
   a. ***Malposition*** of the lacrimal puncta (e.g. secondary to ectropion).
   b. ***Obstruction*** anywhere along the lacrimal drainage system, from the puncta to the nasolacrimal duct.
   c. ***Lacrimal pump failure***, which may occur secondarily to lower lid laxity or weakness of the orbicularis muscle (e.g. facial nerve palsy).

Evaluation of the watering eye

External examination

1. **The marginal tear strip** of both eyes should be examined on the slit-lamp prior to any manipulation of the eyelids or instillation of topical medication, which may prejudice the clinical picture. Many patients with epiphora do not have obvious overflow of tears onto the face but merely show a high marginal tear strip on the affected side.
2. **The eyelids** should be examined for evidence of malposition. Perhaps the commonest cause of lid (and consequently punctal) malposition is ectropion, which may be of involutional, paralytic or cicatricial aetiology. Such ectropion may involve predominantly the pars lacrimalis. Normally the inferior lacrimal punctum is apposed to the globe and not visible without everting the lower lid. A rare cause of epiphora is the *Centurion syndrome*. Patients with this condition manifest epiphora from childhood secondary to anterior malposition of the medial part of the lid with displacement of puncta out of the lacus lacrimalis due to a prominent nasal bridge (Fig. 2.3). Occasionally epiphora may be caused by a large caruncle displacing the inferior punctum away from the globe (Fig. 2.4) or obstruction of the inferior punctum by a fold of redundant conjunctiva (conjunctivochalasis).
3. **The dynamics of eyelid closure** should be evaluated. Normally, the lid margins approximate and the puncta are apposed when the eyes close. In patients with lower lid laxity, one lid may over-ride the other or the puncta may evert (Fig. 2.5).

Fig. 2.4
Large caruncle displacing the inferior punctum

Fig. 2.3
Centurion syndrome

Fig. 2.5
Right upper lid over-riding the lower

4. **The puncta** are best examined on the slit-lamp. Apart from malposition, the puncta may be inflamed, stenosed (Fig. 2.6) or obstructed, sometimes by an eyelash (Fig. 2.7). Canaliculitis is characterized by pouting of the punctum (Fig. 2.8) and expression of pus or concretions on manual canalicular compression with a glass rod. Abnormal findings in children include punctal agenesis, accessory puncta (Fig. 2.9) or a congenital lacrimal fistula.
5. **The lacrimal sac** should then be palpated. Punctal reflux of mucopurulent material on lacrimal compression (Fig. 2.10) is indicative of a mucocele with a patent canalicular system, but with an obstruction either at, or distal to, the lower end of the lacrimal sac. In acute dacryocystitis palpation is severely painful and compression should be avoided. Occasionally, palpation of the sac will reveal a stone or a tumour.
6. **Fluorescein retention test** (fluorescein disappearance test) is performed by instilling fluorescein 2% drops into both conjunctival fornices. Normally, little or no dye remains after 3 minutes. Prolonged retention is indicative of inadequate lacrimal drainage and can be graded from 1 to 4 (Fig. 2.11).

Fig. 2.6
Punctal stenosis associated with mild ectropion

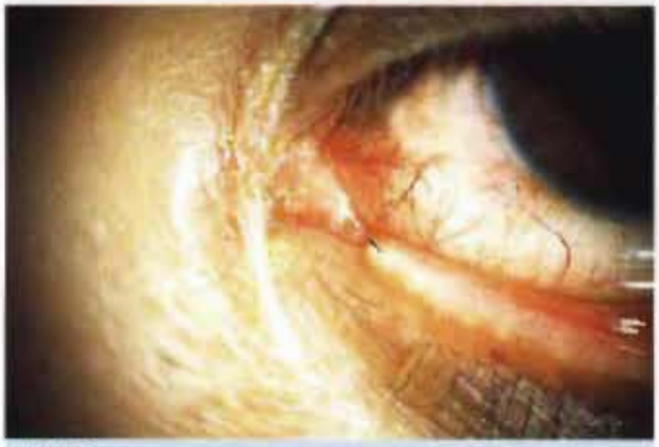

Fig. 2.7
Punctal obstruction by an eyelash

Fig. 2.8
Pouting punctum in chronic canaliculitis

Fig. 2.9
Accessory punctum

Fig. 2.10
Expression of mucopurulent material

Probing and irrigation

This is performed only after ascertaining punctal patency. Under topical anaesthesia, a gently curved, blunt tipped

Fig. 2.11
Prolonged retention of fluorescein-stained tears

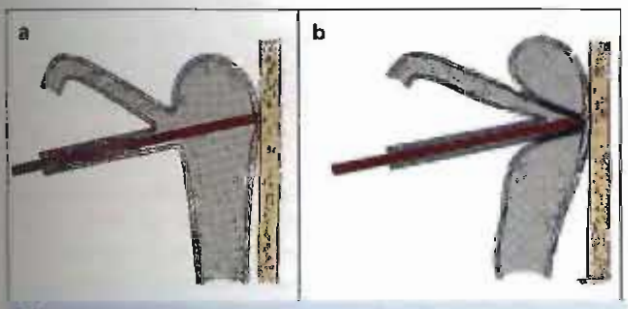

Fig. 2.12
(a) Hard stop; (b) soft stop

lacrimal cannula on a 2 ml saline-filled syringe is inserted into the lower punctum and advanced, following the contour of the canaliculus. An attempt is made to enter the lacrimal sac, the medial wall of which lies against the bone of the lacrimal fossa. The cannula can come either to a hard stop or to a soft stop.

1. **A hard stop** occurs if the cannula enters the lacrimal sac, it comes to a stop at the medial wall of the sac, through which can be felt the rigid lacrimal bone (Fig. 2.12a). This excludes complete obstruction of the canalicular system. The examiner places one finger over the lacrimal fossa and irrigates. If the saline passes into the nose the patient has a patent lacrimal drainage system, which may, however, be stenosed; alternatively there may be subtle lacrimal pump failure. Failure of saline to reach the nose is indicative of total obstruction of the nasolacrimal duct. In this situation, the lacrimal sac will become distended during irrigation and there will also be reflux through the upper punctum. The regurgitated material may be clear, mucoid, mucopurulent or frankly purulent, depending on the contents of the lacrimal sac.
2. **A soft stop** is experienced if the cannula stops at or proximal to the junction of the common canaliculus and the lacrimal sac, i.e. at the lateral wall of the sac. The sac is thus not entered—a spongy feeling is experienced as the cannula presses the soft tissue of the common canaliculus and the lateral wall against the medial wall of the sac and the lacrimal bone behind it (Fig. 2.12b). Irrigation will therefore not cause the sac to distend. In the case of lower canalicular obstruction, there will be reflux of saline through the lower punctum. Reflux through the upper punctum indicates patency of both upper and lower canaliculi, but obstruction of the common canaliculus.

Jones dye testing

This is only indicated in patients with suspected partial obstruction of the drainage system. These patients manifest epiphora, but the lacrimal system can be successfully syringe irrigated. Dye testing is of no value in the context of total obstruction.

1. **The primary test** (Fig. 2.13a) differentiates partial obstruction of the lacrimal passages from primary hypersecretion of tears. First, a drop of 2% fluorescein is instilled into the conjunctival sac. After about 5 minutes, a cotton-tipped bud moistened in a local anaesthetic is inserted under the inferior turbinate at the nasolacrimal duct opening. The results are interpreted as follows:
   a. Positive: fluorescein recovered from the nose indicates patency of the drainage system. Watering is due to primary hypersecretion and no further tests are necessary.
   b. Negative: no dye recovered from the nose indicates a partial obstruction (site unknown) or failure of the

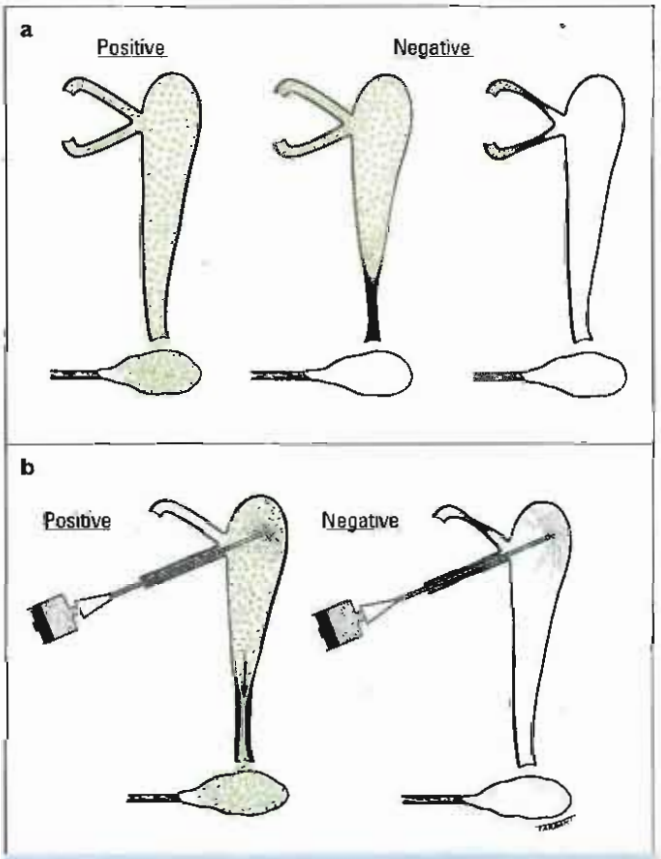

Fig. 2.13
Jones dye testing. (a) primary; (b) secondary

lacrimal pump mechanism. In this situation the secondary dye test is performed immediately.

> ***NB:*** 22% of normal individuals manifest a negative primary Jones test.

2. **The secondary (irrigation) test** (Fig. 2.13b) identifies the probable site of partial obstruction, on the basis of whether the topical fluorescein instilled for the primary test entered the lacrimal sac. Topical anaesthetic is instilled and any residual fluorescein washed out. The drainage system is then irrigated with saline with a cotton-tipped bud under the inferior turbinate.
   a. Positive: fluorescein-stained saline recovered from the nose indicates that fluorescein entered the lacrimal sac, thus confirming functional patency of the upper lacrimal passages. Partial obstruction of the naso-lacrimal duct is inferred.
   b. Negative: unstained saline recovered from the nose indicates that fluorescein did not enter the lacrimal sac. This implies partial obstruction of the upper lacrimal passages (puncta, canaliculi or common canaliculus) or a defective lacrimal pump mechanism.

Contrast dacryocystography

1. **Technique**
   a. The inferior puncta are dilated with a Nettleship punctum dilator.
   b. Plastic catheters are inserted into the inferior canaliculi on either side (alternatively the upper puncta may be used).
   c. Contrast medium, usually 1 ml of Lipiodol, is simultaneously injected on both sides and postero-anterior radiographs are taken (Figs 2.14, 2.15).
   d. Five minutes later an erect oblique film is taken to assess the effect of gravity on tear drainage.

Fig. 2.14
Right dacryocystogram showing free flow of contrast medium into the nose despite mild stenosis of the common canaliculus (Courtesy of R. Welham)

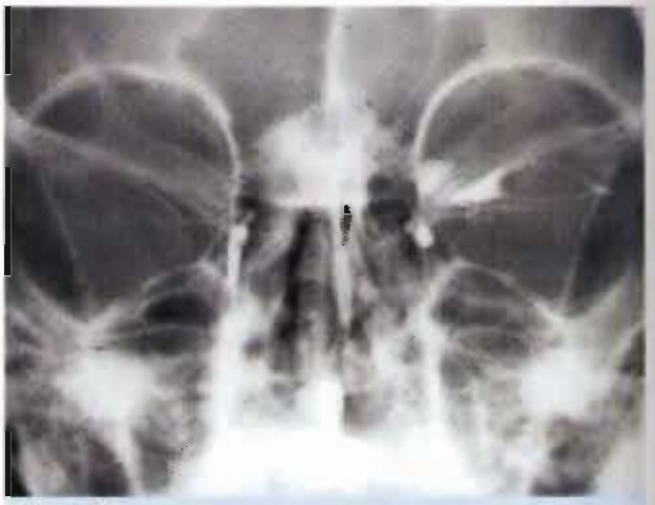

Fig. 2.15
Bilateral dacryocystogram. **(Right)** shows some irregularity of the common canaliculus, although contrast medium passes through an otherwise patent lacrimal system; **(left)** shows complete obstruction high in the sac (Courtesy of R. Welham)

2. **Interpretation.** Failure of dye to reach the nose indicates an anatomical obstruction, the site of which is usually evident. A normal dacryocystogram in the presence of epiphora indicates either partial obstruction or lacrimal pump failure. Dacryocystography is also helpful in the diagnosis of diverticula, fistulae and filling defects caused by stones or tumours.

Lacrimal scintillography

This is a sophisticated test which assesses tear drainage under more physiological conditions than dacryocystography. Although it does not provide the same detailed anatomical visualization as dacryocystography, it is more sensitive in assessing incomplete blocks, especially in the upper part of the lacrimal system. The test is performed as follows:

a. Radionuclide technetium-99 is delivered by a micropipette to the lateral conjunctival sac as a 10 µl drop. The tears are thus labelled with this gamma-emitting radioactive substance.
b. The tracer is imaged by a gamma camera focused on the inner canthus and a sequence of images is recorded over 20 minutes.

Obstruction of lacrimal drainage

Acquired obstruction

Primary punctal stenosis

This occurs in the absence of punctal eversion.

1. **Causes**
   - Idiopathic primary stenosis is by far the most common.
   - Herpes simplex lid infection.
   - Following irradiation of malignant lid tumours.
   - Cicatrizing conjunctivitis and trachoma.
   - Systemic cytotoxic drugs such as 5-fluorouracil and docetaxel.
2. **Treatment** is initially by dilatation of the punctum with a Nettleship dilator (Fig. 2.16). If repeated dilatation is unsuccessful one of the following procedures may be considered:
   a. ***One-snip ampullotomy***, in which a vertical 2 mm snip is made in the posterior wall of the ampulla.
   b. ***Two-snip procedure*** in which both a vertical and a small horizontal cut is made in the ampulla (Fig. 2.17). This yields a larger (Fig. 2.18) and more permanent opening than a one-snip procedure.
   c. ***Laser punctoplasty*** in which the punctum is opened with an argon laser. This method is particularly useful in elderly patients in whom the punctum is occluded by an overgrowth of conjunctival epithelium.
   d. ***Insertion of canalized plugs*** into the inferior punctum.

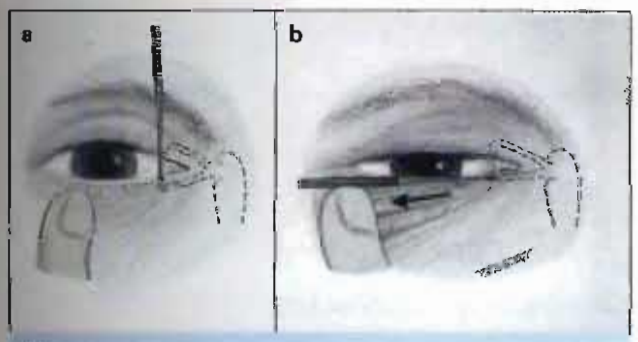

Fig. 2.16
Technique of dilating the inferior punctum

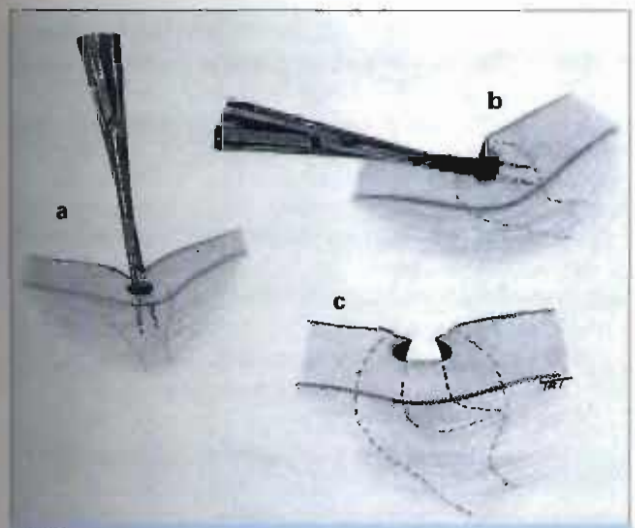

Fig. 2.17
Two-snip procedure for punctal stenosis. (a) Vertical cut; (b) horizontal cut; (c) final result

Fig. 2.18
Appearance following a two-snip procedure

Secondary punctal stenosis

This occurs secondary to punctal eversion (*see* Fig. 2.6). Treatment of pure punctal eversion, unassociated with significant involutional ectropion, is by one of the following:

a. ***Ziegler cautery burns*** are applied to the palpebral conjunctiva, 5 mm below the punctum. Subsequent shrinkage of the cauterized tissue (cicatrization) should invert the punctum.

b. ***Medial conjunctivoplasty*** involves excision of a diamond-shaped piece of tarsoconjunctiva, about 4 mm high and 8 mm wide, parallel with and inferior to the canaliculus and punctum, followed by approximation of the superior and inferior wound margins with sutures (Fig. 2.19). Incorporation of the lower lid retractors in the sutures further aids punctal inversion. Once the punctum is restored to its normal position, it is dilated so that it may remain open when normal tear flow is established. If stenosis recurs, treatment is the same as for primary stenosis.

Canalicular obstruction

1. **Causes** are similar to those of primary punctal obstruction.

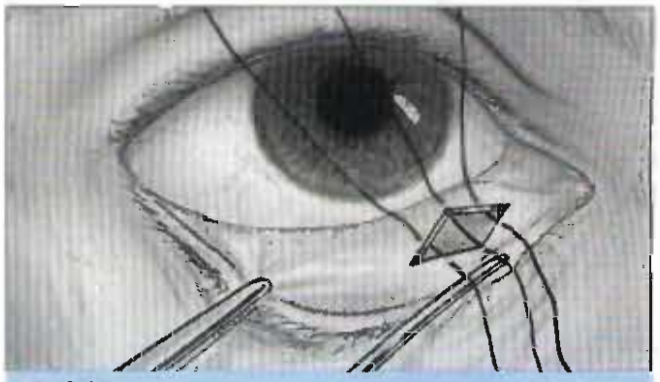

Fig. 2.19
Medial conjunctivoplasty

2. **Treatment** depends on the site and degree of obstruction.
   a. ***Partial*** obstruction of the common or individual canaliculi, or indeed anywhere in the nasolacrimal drainage system, may be treated by intubation. Two ends of a length of silicone tubing are threaded via the superior and inferior puncta, through the lacrimal sac down to the nose, where they are tied (or secured with a special (Watzke) sleeve) and left in situ for 3–6 months (Fig. 2.20).
   b. ***Total individual canalicular obstruction***, with at least 8 mm of patent normal canaliculus between the punctum and obstruction, is treated by anastomosis of the patent part of the canaliculus into the lacrimal sac (canaliculodacryocystorhinostomy—CDCR) and intubation. When the block is less than 8 mm from the punctum treatment involves conjunctivodacryocystorhinostomy and the insertion of a special (Lester Jones) tube (*see* below).
   c. ***Total obstruction of the lateral end*** of the common canaliculus is usually caused by idiopathic peri-canalicular fibrosis, in which the entire common canaliculus is obstructed. Dacryocystography will obviously show failure of filling of the common canaliculus. Treatment involves resection of the obstructed common canaliculus and CDCR. The lacrimal system is then intubated for 3–6 months.
   d. ***Total obstruction of the medial end*** of the common canaliculus is often caused by a thin membrane at its junction with the lumen of the sac, often secondary to chronic dacryocystitis. Dacryocystography will show filling of the common canaliculus. This is treated by DCR and excision of the membrane from its sac aspect (*see* below). The lacrimal system is then intubated for 3–6 months.

Nasolacrimal duct obstruction

1. **Causes**
   - Idiopathic stenosis is by far the most common.
   - Naso-orbital trauma.
   - Wegener granulomatosis.
   - Infiltration by nasopharyngeal tumours.
2. **Treatment** depends on the completeness of obstruction as follows:
   a. ***Complete obstruction*** is treated by DCR.
   b. ***Incomplete obstruction*** may respond to intubation of the lacrimal system with silicone tubes or stents. This should only be performed if the tubes or stents can be passed easily, otherwise a DCR should be done. Some cases may benefit from balloon dilatation (*see* below).

Fig. 2.20
Silicone tube in situ

Dacryolithiasis

Dacryoliths (lacrimal stones) may occur in any part of the lacrimal system, more commonly in males. Although the pathogenesis is unclear, it has been proposed that tear stagnation secondary to inflammatory obstruction may precipitate dacryolith formation and squamous metaplasia of the lacrimal sac epithelium.

1. **Presentation**
   - Dacryoliths are often asymptomatic and may be discovered at the time of DCR.
   - Symptomatic patients usually present in late adulthood in a variety of ways including intermittent epiphora, recurrent attacks of acute dacryocystitis and lacrimal sac distension.
2. **Signs**
   - The lacrimal sac is distended and relatively firm, but is not inflamed and tender as in acute dacryocystitis.
   - Mucus reflux on pressure may or may not be present.
3. **Treatment** involves massage, lacrimal irrigation and probing; DCR may be required for complete obstruction.

Congenital obstruction

Nasolacrimal duct obstruction

This is perhaps better termed delayed canalization of the nasolacrimal duct, since it often resolves spontaneously. The lower end of the nasolacrimal duct (at the valve of Hasner) is the last portion of the lacrimal drainage system to canalize, complete canalization usually occurring soon after birth. However, up to 20% of children manifest evidence of naso-lacrimal obstruction in the first year of life.

1. **Signs**
   - Epiphora and matting of lashes may be constant or intermittent when the child has a cold or upper respiratory tract infection (Fig. 2.21).
   - Gentle pressure over the lacrimal sac causes reflux of purulent material from the puncta.
   - Acute dacryocystitis is uncommon (Fig. 2.22).
2. **Differential diagnosis** of other congenital causes of a watering eye include punctal atresia and fistulae between the sac and skin.

NB: It is important to exclude congenital glaucoma in an infant with a watering eye.

Fig. 2.21
Sticky eye due to delayed canalization of the nasolacrimal duct

Fig. 2.22
Acute dacryocystitis secondary to delayed canalization of the nasolacrimal duct (Courtesy of R. Welham)

3. Treatment

a. Massage of the lacrimal sac increases the hydrostatic pressure and may rupture the membranous obstruction. In performing this manoeuvre, the index finger is placed over the common canaliculus to block reflux through the puncta and then massaged firmly downwards. Ten strokes should be applied four times a day. Massage should be accompanied by lid hygiene; however, topical antibiotics should be reserved for superadded bacterial conjunctivitis, which is surprisingly uncommon.

b. Probing of the lacrimal system should be delayed until the age of 12 months because spontaneous canalization occurs in about 95% of cases. Probing performed within the first 2 years of life has a very high success rate, but thereafter the efficacy decreases. It should be carried out under a general anaesthetic and preferably through the upper punctum (Fig. 2.23). The rationale is to manually overcome the obstructive membrane at the Hasner valve. After probing, the lacrimal system is irrigated with saline labelled with fluorescein. If fluorescein can be recovered by aspiration from the pharynx, successful probing is confirmed. Postoperative antibiotic drops are used q.i.d. for 1 week. If, after 6 weeks, there is no improvement, probing should be repeated. Nasal endoscopic monitoring of probing is recommended, especially for repeated probing, to detect anatomical abnormalities and ensure correct probe position.

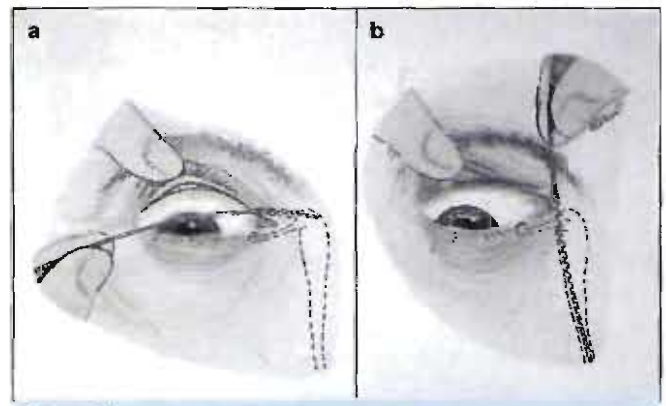

Fig. 2.23
Technique of probing of the nasolacrimal duct

4. Results. Ninety per cent of children are cured by the first probing and a further 6% by the second. Failure is usually the result of abnormal anatomy, which can usually be recognized by difficulty in passing the probe and subsequent non-patency of the lacrimal drainage system on irrigation. If symptoms persist despite two technically satisfactory probings, temporary intubation with fine silastic tubes or balloon dilatation of the nasolacrimal duct may effect a cure. Patients who fail to respond to such measures can be treated with DCR performed between the ages of 3 and 4 years, provided the obstruction is distal to the lacrimal sac.

Fig. 2.24
Amniontocele (Courtesy of R. Welham)

Congenital dacryocele

A congenital dacryocele (amniontocele) is a collection of amniotic fluid or mucus in the lacrimal sac caused by an imperforate Hasner valve.

1. **Presentation** is perinatal with a bluish cystic swelling at or below the medial canthal area, accompanied by epiphora (Fig. 2.24).
2. **Signs**. A tense lacrimal sac which is initially filled with mucus but may become secondarily infected.

> ***NB:*** It should not be mistaken for an encephalocele, which is characterized by a pulsatile swelling above the medial canthal tendon.

3. **Treatment** is initially conservative but if this fails probing should not be delayed.

Principles of lacrimal surgery

Conventional DCR

This is indicated for obstruction beyond the medial opening of the common canaliculus (i.e. the canalicular system is patent). In principle this operation involves anastomosing the lacrimal sac to the nasal mucosa of the middle nasal meatus. The procedure is performed under general hypotensive anaesthesia.

1. **Technique**
   a. The middle nasal mucosa is packed with sterile ribbon gauze soaked in 2% lignocaine with 1:200,000 adrenaline, to achieve vasoconstriction of the mucosa.
   b. A straight vertical incision is made 10 mm medial to the inner canthus, avoiding the angular vein (Fig. 2.25a).
   c. The anterior lacrimal crest is exposed by blunt dissection and the superficial portion of the medial palpebral ligament divided.
   d. The periosteum is divided from the spine on the anterior lacrimal crest to the fundus of the sac and reflected forwards. The sac is reflected laterally from the lacrimal fossa (Fig. 2.25b).
   e. The anterior lacrimal crest and the bone from the lacrimal fossa are removed (Fig. 2.25c).
   f. A probe is introduced into the lacrimal sac through the lower canaliculus and the sac is incised in an 'H-shaped' manner to create two flaps.
   g. A vertical incision is made in the nasal mucosa to create anterior and posterior flaps (Fig. 2.25d).
   h. The posterior flaps are sutured (Fig. 2.25e).
   i. The anterior flaps are sutured (Fig. 2.25f).
   j. The medial canthal tendon is resutured to the periosteum and the skin incision closed with interrupted sutures.
2. **Results** in experienced hands are excellent with a success rate of over 90%.
3. **Causes of failure** include inadequate size and position of the ostium, unrecognized common canalicular obstruction, scarring and the 'sump syndrome', in which the surgical opening in the lacrimal bone is too small and too high. There is thus a dilated lacrimal sac lateral to and below the level of the inferior margin of the ostium, in which secretions collect, unable to gain access to the ostium and thence the nasal cavity.
4. **Potential complications** include cutaneous scarring, injury to medial canthal structures, haemorrhage, cellulitis and cerebrospinal fluid rhinorrhoea, if the subarachnoid space is inadvertently entered.

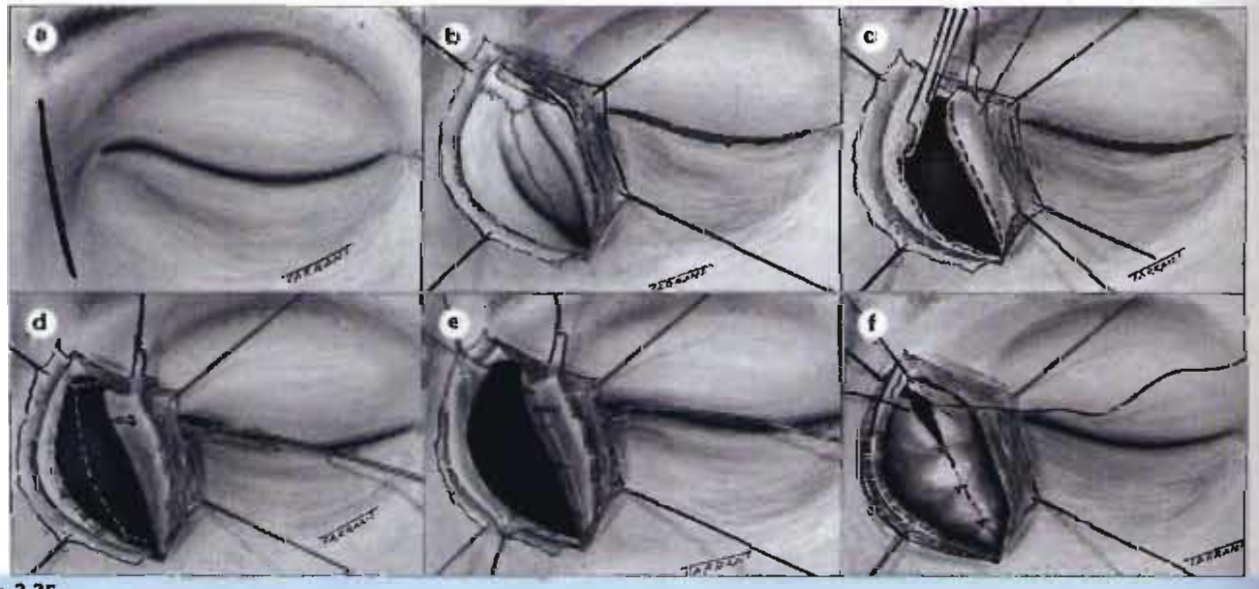

Fig. 2.25
Technique of dacryocystorhinostomy (see text)

Endoscopic DCR

This may be considered for obstruction beyond the medial opening of the common canaliculus, particularly following failed conventional DCR. The procedure can be performed either under general anaesthesia (without hypotension) or local anaesthesia. Advantages over conventional DCR include the lack of skin incision, shorter operating time, lower risk of interfering with the physiological lacrimal pump mechanism, minimal blood loss and no risk of cerebrospinal fluid rhinorrhoea.

1. **Technique.** A slender light pipe is passed through the lacrimal puncta and canaliculi into the lacrimal sac and viewed from within the nasal cavity with an endoscope. The remainder of the procedure is performed from within the nasal cavity.
   a. The mucosa over the frontal process of the maxilla is stripped.
   b. A part of the nasal process of the maxilla is removed.
   c. The lacrimal bone is broken off piecemeal.
   d. The lacrimal sac is opened.
   e. Silicone tubes are passed through the upper and lower puncta, pulled out through the ostium and tied within the nose.
2. **Results.** The success rate is about 85%.

Endolaser DCR

Performed with a holmium:YAG laser, this is a quick procedure which can be carried out under local anaesthesia. It is therefore particularly suitable for elderly patients. The success rate is only about 70% but because normal anatomy is not disrupted it does not prejudice subsequent surgical intervention in the cases that fail.

Lester Jones tube

Insertion of a Lester Jones tube is indicated when there is absence of canalicular function, either due to obstruction less than 8 mm from the puncta, or due to lacrimal pump failure.

a. A DCR is performed as far as suturing the posterior flaps.
b. The caruncle is partially excised.
c. A stab incision is made with a Graefe knife from a point about 2 mm behind the inner canthus (under the former caruncle) in a medial direction, so that the tip of the knife emerges just behind the anterior flap of the lacrimal sac (Fig. 2.26a).
d. The tract is enlarged sufficiently with a microtrephine to allow the introduction of a polythene tube (Fig. 2.26b).
e. The incision is sutured as for a DCR.
f. After 2 weeks the polythene tube is replaced by a glass tube.

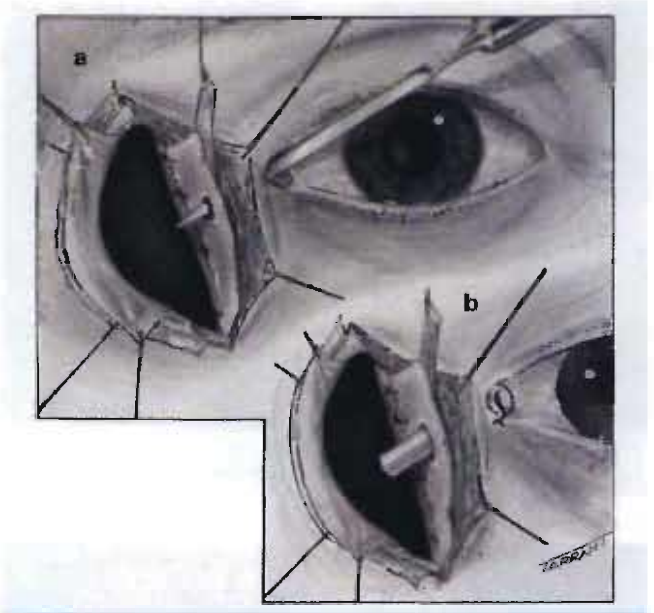

Fig. 2.26
Technique of Lester Jones tube insertion (see text)

Balloon dacryocystoplasty

This may be a satisfactory primary treatment for adults with partial nasolacrimal duct obstruction who do not exhibit signs of chronic infection.

Infections of lacrimal passages

Chronic canaliculitis

Chronic canaliculitis is an uncommon condition, frequently caused by *Actinomyces*, which are anaerobic Gram-positive bacteria. While a diverticulum or obstruction of the canaliculus can promote anaerobic bacterial growth secondary to stasis, in most cases there is no identifiable predisposition.

1. **Presentation** is with unilateral epiphora associated with chronic mucopurulent conjunctivitis, refractory to conventional treatment.
2. **Signs**
   - Pericanalicular inflammation is characterized by oedema of the canaliculus (Fig. 2.27) and a 'pouting' punctum best seen with the slit-lamp (Fig. 2.28).
   - Concretions consisting of sulphur granules are expressed on canalicular compression with a glass rod (Fig. 2.29).

> ***NB:*** In contrast to dacryocystitis, there is no nasolacrimal duct obstruction, lacrimal sac distension or inflammation.

3. **Treatment**
   a. Topical antibiotics such as ciprofloxacin q.i.d. for 10 days may be tried initially but are rarely curative.

Fig. 2.27
Oedema of the left upper canaliculus in chronic canaliculitis

Fig. 2.28
Pouting of the punctum in chronic canaliculitis

Fig. 2.29
Expressed concretions in chronic canaliculitis

b. Canaliculotomy (Fig. 2.30) involving a linear incision into the conjunctival side of the canaliculus is the most effective treatment, although occasionally it may result in scarring and interference with canalicular function.

Fig. 2.30
Exposure of large concretions following canaliculotomy in chronic canaliculitis

Dacryocystitis

Infection of the lacrimal sac is usually secondary to obstruction of the nasolacrimal duct. It may be acute or chronic and is most commonly caused by staphylococci.

Acute dacryocystitis

1. **Presentation** is with subacute onset of pain, redness and swelling at the medial canthus and epiphora.

Fig. 2.31
Acute dacryocystitis

2. **Signs.** A very tender, red, tense swelling at the medial canthus which may be associated with preseptal cellulitis in severe cases (Fig. 2.31).
3. **Treatment**
   a. *Initial* treatment involves the application of local warmth and oral antibiotics such as flucloxacillin.

> *NB:* Irrigation and probing should not be performed.

   b. *Incision and drainage.* The infection may sometimes extend outside the sac to produce an abscess in the perilacrimal soft tissue (lacrimal abscess). If pus points and the abscess threatens to drain spontaneously (Fig. 2.32), incision and drainage may be considered. This, however, carries a risk of the development of a lacrimal fistula, which may serve as a conduit for tears from the lumen of the lacrimal sac to the skin surface.
   c. *DCR* is usually necessary after the acute infection has been controlled and should not be delayed because of the risk of recurrent infection.

Fig. 2.32
Lacrimal sac abscess

Fig. 2.33
Mucocele

Chronic dacryocystitis

1. **Presentation** is with epiphora which may be associated with a chronic or recurrent unilateral conjunctivitis.
2. **Signs.** A painless swelling at the inner canthus caused by a mucocele (Fig. 2.33). Obvious swelling may be absent, although pressure over the sac commonly still results in reflux of mucopurulent material through the canaliculi (*see* Fig. 2.10).

> *NB:* It is often wise to postpone intraocular surgery until lacrimal infection has been treated, owing to the grave risk of endophthalmitis.

3. **Treatment** is with DCR.

CHAPTER 2

Lacrimal Drainage System

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Introduction

Applied anatomy

The lacrimal drainage system consists of the following structures (Fig. 2.1):

1. **The puncta** are located at the posterior edge of the lid margin, at the junction of the lash-bearing lateral five-sixths (pars ciliaris) and the non-ciliated medial one-sixth (pars lacrimalis) of each lid. Normally they face slightly posteriorly and can be inspected by everting the medial aspect of the lids. Treatment of excessive watering caused by punctal stenosis or malposition is relatively straightforward.
2. **The canaliculi** pass vertically from the lid margin (the ampullae) for about 2 mm. They then turn medially and run horizontally for about 8 mm to reach the lacrimal sac. The superior and inferior canaliculi most often unite to form the common canaliculus, which opens into the lateral wall of the lacrimal sac. In some individuals, each canaliculus opens separately. A small flap of mucosa (valve of Rosenmuller) overhangs the junction of the common canaliculus and the lacrimal sac and prevents reflux of tears into the canaliculi. Treatment of canalicular obstruction is frequently complicated.
3. **The lacrimal sac** is about 10 mm long and lies in the lacrimal fossa between the anterior and posterior lacrimal crests. The lacrimal bone and the frontal process of the maxilla separate the lacrimal sac from the middle meatus of the nasal cavity. In a dacryocystorhinostomy (DCR) an anastomosis is created between the sac and the nasal mucosa to bypass an obstruction in the nasolacrimal duct.
4. **The nasolacrimal duct** is about 12 mm long and is the inferior continuation of the lacrimal sac. It descends and angles slightly laterally and posteriorly to open into the inferior nasal meatus, lateral to and below the inferior turbinate. The opening of the duct is partially covered by a mucosal fold (valve of Hasner). Obstruction of the duct may cause a secondary distension of the sac.

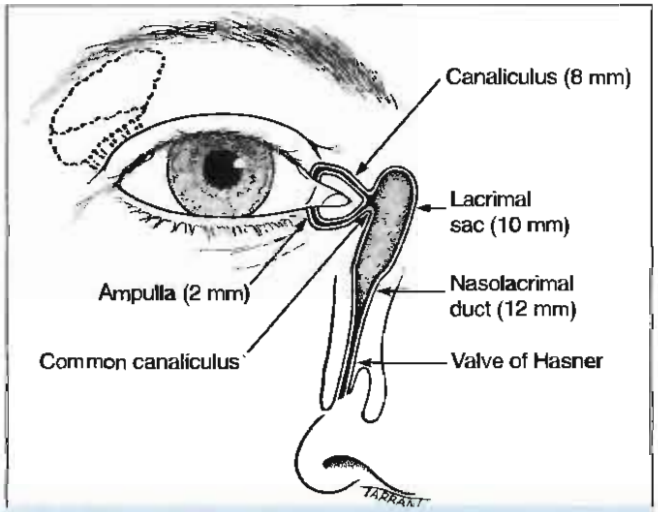

Fig. 2.1
Anatomy of the lacrimal drainage system

Applied physiology

Tears secreted by the main and accessory lacrimal glands pass laterally across the ocular surface. A variable amount of the aqueous component of the tear film is lost by evaporation. This is related to the size of the palpebral aperture, the blink rate, ambient temperature and humidity. The remainder of the tears drain as follows (Fig. 2.2):

1. Tears flow along the upper and lower marginal strips and enter the upper and lower canaliculi by capillarity and also possibly by suction. About 70% of tears drain through the lower canaliculus and the remainder through the upper (Fig. 2.2a).
2. With each blink, the pretarsal orbicularis oculi compresses the ampullae, shortens the horizontal canaliculi and moves the puncta medially (Fig. 2.2b). Simultaneously, the lacrimal part of the orbicularis oculi, which is attached to the fascia of the lacrimal sac, contracts and expands the sac, thereby creating a negative pressure which sucks the tears from the canaliculi into the sac.
3. When the eyes open the muscles relax, the sac collapses and a positive pressure is created which forces the tears

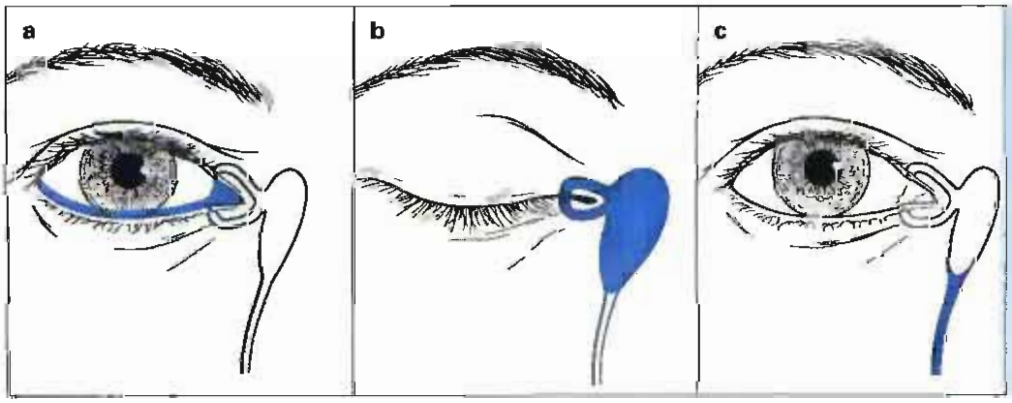

Fig. 2.2
Physiology of the lacrimal pump mechanism

down the nasolacrimal duct into the nose (Fig. 2.2c). Gravity also plays a role. The puncta move laterally, the canaliculi lengthen and fill with tears.

Causes of watering

Overflow of tears may represent lacrimation or epiphora.

1. **Lacrimation** (hyperlacrimation) is caused by reflex lacrimal hypersecretion secondary to ocular inflammation or surface disease. In these cases watering is associated with symptoms of the underlying cause and treatment is usually medical.
2. **Epiphora** is due to compromise of lacrimal drainage. It is exacerbated by a cold and windy atmosphere, and is least in a warm dry room. It may be caused by:
   a. ***Malposition*** of the lacrimal puncta (e.g. secondary to ectropion).
   b. ***Obstruction*** anywhere along the lacrimal drainage system, from the puncta to the nasolacrimal duct.
   c. ***Lacrimal pump failure***, which may occur secondarily to lower lid laxity or weakness of the orbicularis muscle (e.g. facial nerve palsy).

Evaluation of the watering eye

External examination

1. **The marginal tear strip** of both eyes should be examined on the slit-lamp prior to any manipulation of the eyelids or instillation of topical medication, which may prejudice the clinical picture. Many patients with epiphora do not have obvious overflow of tears onto the face but merely show a high marginal tear strip on the affected side.
2. **The eyelids** should be examined for evidence of malposition. Perhaps the commonest cause of lid (and consequently punctal) malposition is ectropion, which may be of involutional, paralytic or cicatricial aetiology. Such ectropion may involve predominantly the pars lacrimalis. Normally the inferior lacrimal punctum is apposed to the globe and not visible without everting the lower lid. A rare cause of epiphora is the *Centurion syndrome*. Patients with this condition manifest epiphora from childhood secondary to anterior malposition of the medial part of the lid with displacement of puncta out of the lacus lacrimalis due to a prominent nasal bridge (Fig. 2.3). Occasionally epiphora may be caused by a large caruncle displacing the inferior punctum away from the globe (Fig. 2.4) or obstruction of the inferior punctum by a fold of redundant conjunctiva (conjunctivochalasis).
3. **The dynamics of eyelid closure** should be evaluated. Normally, the lid margins approximate and the puncta are apposed when the eyes close. In patients with lower lid laxity, one lid may over-ride the other or the puncta may evert (Fig. 2.5).

Fig. 2.4
Large caruncle displacing the inferior punctum

Fig. 2.3
Centurion syndrome

Fig. 2.5
Right upper lid over-riding the lower

4. **The puncta** are best examined on the slit-lamp. Apart from malposition, the puncta may be inflamed, stenosed (Fig. 2.6) or obstructed, sometimes by an eyelash (Fig. 2.7). Canaliculitis is characterized by pouting of the punctum (Fig. 2.8) and expression of pus or concretions on manual canalicular compression with a glass rod. Abnormal findings in children include punctal agenesis, accessory puncta (Fig. 2.9) or a congenital lacrimal fistula.
5. **The lacrimal sac** should then be palpated. Punctal reflux of mucopurulent material on lacrimal compression (Fig. 2.10) is indicative of a mucocele with a patent canalicular system, but with an obstruction either at, or distal to, the lower end of the lacrimal sac. In acute dacryocystitis palpation is severely painful and compression should be avoided. Occasionally, palpation of the sac will reveal a stone or a tumour.
6. **Fluorescein retention test** (fluorescein disappearance test) is performed by instilling fluorescein 2% drops into both conjunctival fornices. Normally, little or no dye remains after 3 minutes. Prolonged retention is indicative of inadequate lacrimal drainage and can be graded from 1 to 4 (Fig. 2.11).

Fig. 2.6
Punctal stenosis associated with mild ectropion

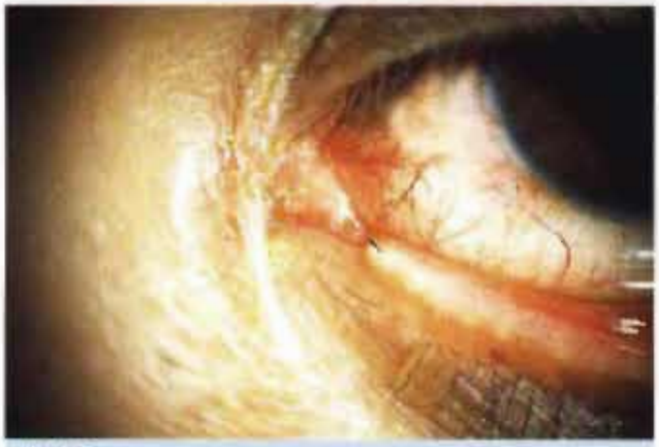

Fig. 2.7
Punctal obstruction by an eyelash

Fig. 2.8
Pouting punctum in chronic canaliculitis

Fig. 2.9
Accessory punctum

Fig. 2.10
Expression of mucopurulent material

Probing and irrigation

This is performed only after ascertaining punctal patency. Under topical anaesthesia, a gently curved, blunt tipped

Fig. 2.11
Prolonged retention of fluorescein-stained tears

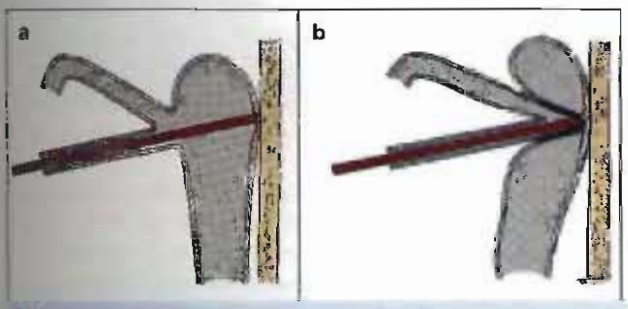

Fig. 2.12
(a) Hard stop; (b) soft stop

lacrimal cannula on a 2 ml saline-filled syringe is inserted into the lower punctum and advanced, following the contour of the canaliculus. An attempt is made to enter the lacrimal sac, the medial wall of which lies against the bone of the lacrimal fossa. The cannula can come either to a hard stop or to a soft stop.

1. **A hard stop** occurs if the cannula enters the lacrimal sac, it comes to a stop at the medial wall of the sac, through which can be felt the rigid lacrimal bone (Fig. 2.12a). This excludes complete obstruction of the canalicular system. The examiner places one finger over the lacrimal fossa and irrigates. If the saline passes into the nose the patient has a patent lacrimal drainage system, which may, however, be stenosed; alternatively there may be subtle lacrimal pump failure. Failure of saline to reach the nose is indicative of total obstruction of the nasolacrimal duct. In this situation, the lacrimal sac will become distended during irrigation and there will also be reflux through the upper punctum. The regurgitated material may be clear, mucoid, mucopurulent or frankly purulent, depending on the contents of the lacrimal sac.
2. **A soft stop** is experienced if the cannula stops at or proximal to the junction of the common canaliculus and the lacrimal sac, i.e. at the lateral wall of the sac. The sac is thus not entered—a spongy feeling is experienced as the cannula presses the soft tissue of the common canaliculus and the lateral wall against the medial wall of the sac and the lacrimal bone behind it (Fig. 2.12b). Irrigation will therefore not cause the sac to distend. In the case of lower canalicular obstruction, there will be reflux of saline through the lower punctum. Reflux through the upper punctum indicates patency of both upper and lower canaliculi, but obstruction of the common canaliculus.

Jones dye testing

This is only indicated in patients with suspected partial obstruction of the drainage system. These patients manifest epiphora, but the lacrimal system can be successfully syringe irrigated. Dye testing is of no value in the context of total obstruction.

1. **The primary test** (Fig. 2.13a) differentiates partial obstruction of the lacrimal passages from primary hypersecretion of tears. First, a drop of 2% fluorescein is instilled into the conjunctival sac. After about 5 minutes, a cotton-tipped bud moistened in a local anaesthetic is inserted under the inferior turbinate at the nasolacrimal duct opening. The results are interpreted as follows:
   a. Positive: fluorescein recovered from the nose indicates patency of the drainage system. Watering is due to primary hypersecretion and no further tests are necessary.
   b. Negative: no dye recovered from the nose indicates a partial obstruction (site unknown) or failure of the

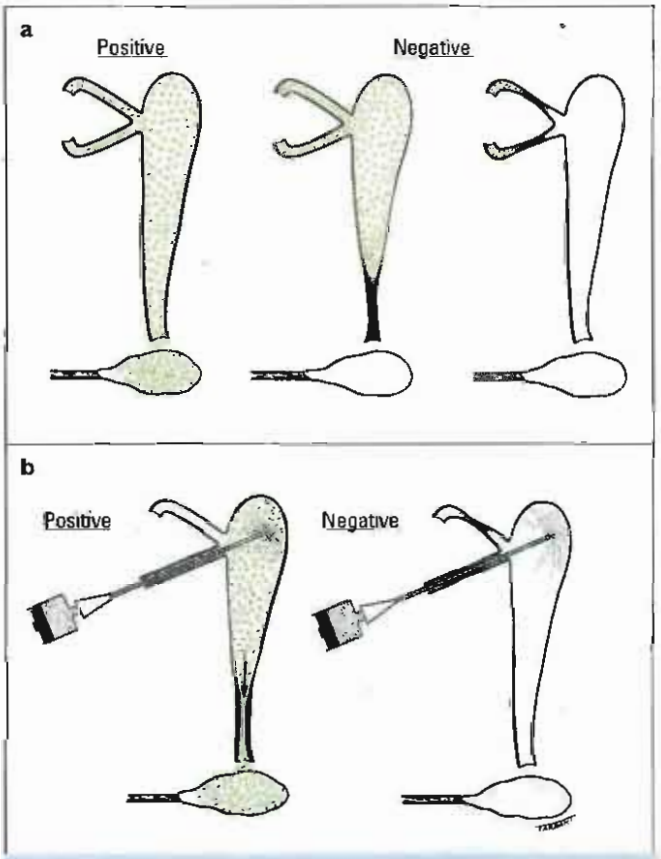

Fig. 2.13
Jones dye testing. (a) primary; (b) secondary

lacrimal pump mechanism. In this situation the secondary dye test is performed immediately.

> ***NB:*** 22% of normal individuals manifest a negative primary Jones test.

2. **The secondary (irrigation) test** (Fig. 2.13b) identifies the probable site of partial obstruction, on the basis of whether the topical fluorescein instilled for the primary test entered the lacrimal sac. Topical anaesthetic is instilled and any residual fluorescein washed out. The drainage system is then irrigated with saline with a cotton-tipped bud under the inferior turbinate.
   a. Positive: fluorescein-stained saline recovered from the nose indicates that fluorescein entered the lacrimal sac, thus confirming functional patency of the upper lacrimal passages. Partial obstruction of the naso-lacrimal duct is inferred.
   b. Negative: unstained saline recovered from the nose indicates that fluorescein did not enter the lacrimal sac. This implies partial obstruction of the upper lacrimal passages (puncta, canaliculi or common canaliculus) or a defective lacrimal pump mechanism.

Contrast dacryocystography

1. **Technique**
   a. The inferior puncta are dilated with a Nettleship punctum dilator.
   b. Plastic catheters are inserted into the inferior canaliculi on either side (alternatively the upper puncta may be used).
   c. Contrast medium, usually 1 ml of Lipiodol, is simultaneously injected on both sides and postero-anterior radiographs are taken (Figs 2.14, 2.15).
   d. Five minutes later an erect oblique film is taken to assess the effect of gravity on tear drainage.

Fig. 2.14
Right dacryocystogram showing free flow of contrast medium into the nose despite mild stenosis of the common canaliculus (Courtesy of R. Welham)

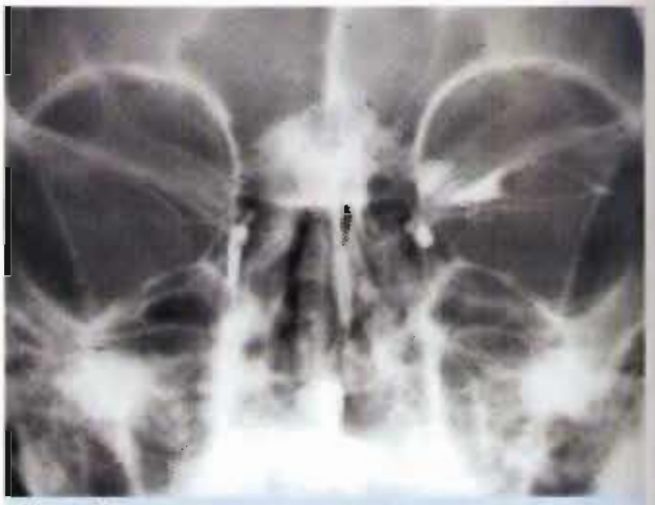

Fig. 2.15
Bilateral dacryocystogram. **(Right)** shows some irregularity of the common canaliculus, although contrast medium passes through an otherwise patent lacrimal system; **(left)** shows complete obstruction high in the sac (Courtesy of R. Welham)

2. **Interpretation.** Failure of dye to reach the nose indicates an anatomical obstruction, the site of which is usually evident. A normal dacryocystogram in the presence of epiphora indicates either partial obstruction or lacrimal pump failure. Dacryocystography is also helpful in the diagnosis of diverticula, fistulae and filling defects caused by stones or tumours.

Lacrimal scintillography

This is a sophisticated test which assesses tear drainage under more physiological conditions than dacryocystography. Although it does not provide the same detailed anatomical visualization as dacryocystography, it is more sensitive in assessing incomplete blocks, especially in the upper part of the lacrimal system. The test is performed as follows:

a. Radionuclide technetium-99 is delivered by a micropipette to the lateral conjunctival sac as a 10 µl drop. The tears are thus labelled with this gamma-emitting radioactive substance.
b. The tracer is imaged by a gamma camera focused on the inner canthus and a sequence of images is recorded over 20 minutes.

Obstruction of lacrimal drainage

Acquired obstruction

Primary punctal stenosis

This occurs in the absence of punctal eversion.

1. **Causes**
   - Idiopathic primary stenosis is by far the most common.
   - Herpes simplex lid infection.
   - Following irradiation of malignant lid tumours.
   - Cicatrizing conjunctivitis and trachoma.
   - Systemic cytotoxic drugs such as 5-fluorouracil and docetaxel.
2. **Treatment** is initially by dilatation of the punctum with a Nettleship dilator (Fig. 2.16). If repeated dilatation is unsuccessful one of the following procedures may be considered:
   a. ***One-snip ampullotomy***, in which a vertical 2 mm snip is made in the posterior wall of the ampulla.
   b. ***Two-snip procedure*** in which both a vertical and a small horizontal cut is made in the ampulla (Fig. 2.17). This yields a larger (Fig. 2.18) and more permanent opening than a one-snip procedure.
   c. ***Laser punctoplasty*** in which the punctum is opened with an argon laser. This method is particularly useful in elderly patients in whom the punctum is occluded by an overgrowth of conjunctival epithelium.
   d. ***Insertion of canalized plugs*** into the inferior punctum.

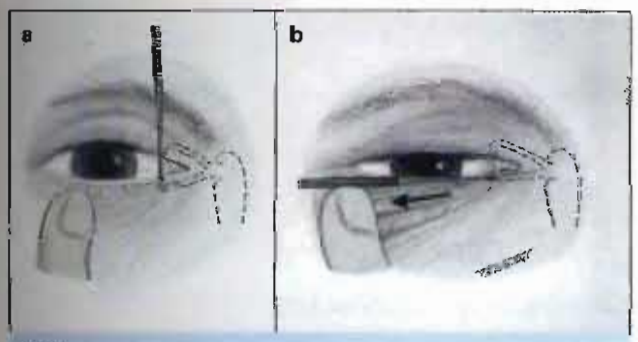

Fig. 2.16
Technique of dilating the inferior punctum

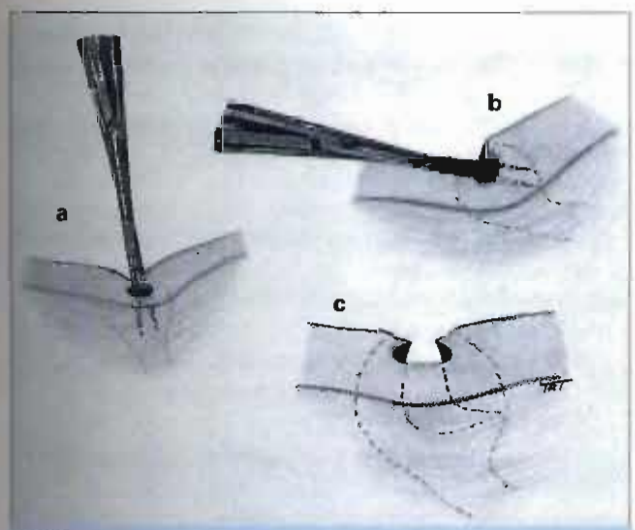

Fig. 2.17
Two-snip procedure for punctal stenosis. (a) Vertical cut; (b) horizontal cut; (c) final result

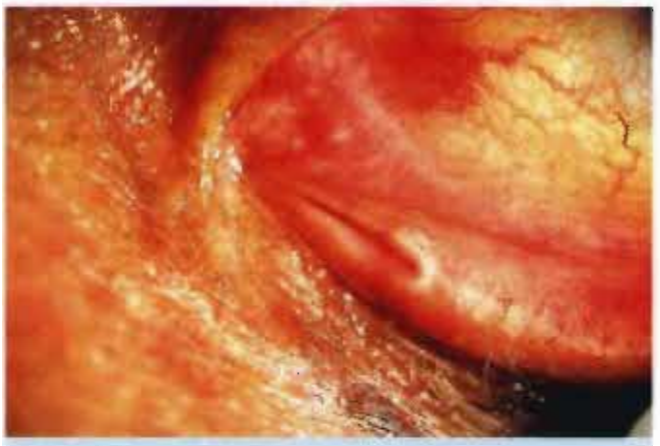

Fig. 2.18
Appearance following a two-snip procedure

Secondary punctal stenosis

This occurs secondary to punctal eversion (*see* Fig. 2.6). Treatment of pure punctal eversion, unassociated with significant involutional ectropion, is by one of the following:

a. ***Ziegler cautery burns*** are applied to the palpebral conjunctiva, 5 mm below the punctum. Subsequent shrinkage of the cauterized tissue (cicatrization) should invert the punctum.

b. ***Medial conjunctivoplasty*** involves excision of a diamond-shaped piece of tarsoconjunctiva, about 4 mm high and 8 mm wide, parallel with and inferior to the canaliculus and punctum, followed by approximation of the superior and inferior wound margins with sutures (Fig. 2.19). Incorporation of the lower lid retractors in the sutures further aids punctal inversion. Once the punctum is restored to its normal position, it is dilated so that it may remain open when normal tear flow is established. If stenosis recurs, treatment is the same as for primary stenosis.

Canalicular obstruction

1. **Causes** are similar to those of primary punctal obstruction.

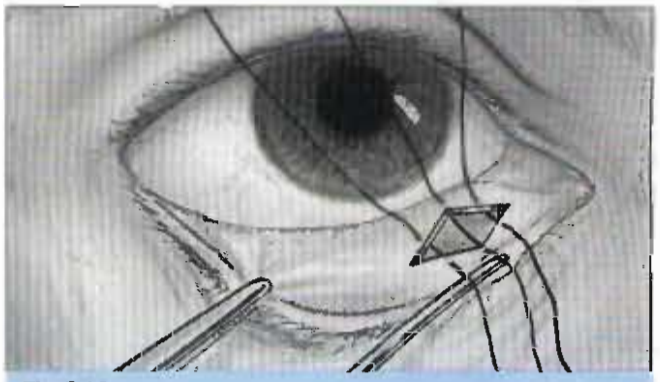

Fig. 2.19
Medial conjunctivoplasty

2. **Treatment** depends on the site and degree of obstruction.
   a. ***Partial*** obstruction of the common or individual canaliculi, or indeed anywhere in the nasolacrimal drainage system, may be treated by intubation. Two ends of a length of silicone tubing are threaded via the superior and inferior puncta, through the lacrimal sac down to the nose, where they are tied (or secured with a special (Watzke) sleeve) and left in situ for 3–6 months (Fig. 2.20).
   b. ***Total individual canalicular obstruction,*** with at least 8 mm of patent normal canaliculus between the punctum and obstruction, is treated by anastomosis of the patent part of the canaliculus into the lacrimal sac (canaliculodacryocystorhinostomy—CDCR) and intubation. When the block is less than 8 mm from the punctum treatment involves conjunctivodacryocystorhinostomy and the insertion of a special (Lester Jones) tube (*see* below).
   c. ***Total obstruction of the lateral end*** of the common canaliculus is usually caused by idiopathic peri-canalicular fibrosis, in which the entire common canaliculus is obstructed. Dacryocystography will obviously show failure of filling of the common canaliculus. Treatment involves resection of the obstructed common canaliculus and CDCR. The lacrimal system is then intubated for 3–6 months.
   d. ***Total obstruction of the medial end*** of the common canaliculus is often caused by a thin membrane at its junction with the lumen of the sac, often secondary to chronic dacryocystitis. Dacryocystography will show filling of the common canaliculus. This is treated by DCR and excision of the membrane from its sac aspect (*see* below). The lacrimal system is then intubated for 3–6 months.

Nasolacrimal duct obstruction

1. **Causes**
   - Idiopathic stenosis is by far the most common.
   - Naso-orbital trauma.

Fig. 2.20
Silicone tube in situ

   - Wegener granulomatosis.
   - Infiltration by nasopharyngeal tumours.
2. **Treatment** depends on the completeness of obstruction as follows:
   a. ***Complete obstruction*** is treated by DCR.
   b. ***Incomplete obstruction*** may respond to intubation of the lacrimal system with silicone tubes or stents. This should only be performed if the tubes or stents can be passed easily, otherwise a DCR should be done. Some cases may benefit from balloon dilatation (*see* below).

Dacryolithiasis

Dacryoliths (lacrimal stones) may occur in any part of the lacrimal system, more commonly in males. Although the pathogenesis is unclear, it has been proposed that tear stagnation secondary to inflammatory obstruction may precipitate dacryolith formation and squamous metaplasia of the lacrimal sac epithelium.

1. **Presentation**
   - Dacryoliths are often asymptomatic and may be discovered at the time of DCR.
   - Symptomatic patients usually present in late adulthood in a variety of ways including intermittent epiphora, recurrent attacks of acute dacryocystitis and lacrimal sac distension.
2. **Signs**
   - The lacrimal sac is distended and relatively firm, but is not inflamed and tender as in acute dacryocystitis.
   - Mucus reflux on pressure may or may not be present.
3. **Treatment** involves massage, lacrimal irrigation and probing; DCR may be required for complete obstruction.

Congenital obstruction

Nasolacrimal duct obstruction

This is perhaps better termed delayed canalization of the nasolacrimal duct, since it often resolves spontaneously. The lower end of the nasolacrimal duct (at the valve of Hasner) is the last portion of the lacrimal drainage system to canalize, complete canalization usually occurring soon after birth. However, up to 20% of children manifest evidence of naso-lacrimal obstruction in the first year of life.

1. **Signs**
   - Epiphora and matting of lashes may be constant or intermittent when the child has a cold or upper respiratory tract infection (Fig. 2.21).
   - Gentle pressure over the lacrimal sac causes reflux of purulent material from the puncta.
   - Acute dacryocystitis is uncommon (Fig. 2.22).
2. **Differential diagnosis** of other congenital causes of a watering eye include punctal atresia and fistulae between the sac and skin.

NB: It is important to exclude congenital glaucoma in an infant with a watering eye.

Fig. 2.21
Sticky eye due to delayed canalization of the nasolacrimal duct

Fig. 2.22
Acute dacryocystitis secondary to delayed canalization of the nasolacrimal duct (Courtesy of R. Welham)

3. Treatment

a. Massage of the lacrimal sac increases the hydrostatic pressure and may rupture the membranous obstruction. In performing this manoeuvre, the index finger is placed over the common canaliculus to block reflux through the puncta and then massaged firmly downwards. Ten strokes should be applied four times a day. Massage should be accompanied by lid hygiene; however, topical antibiotics should be reserved for superadded bacterial conjunctivitis, which is surprisingly uncommon.

b. Probing of the lacrimal system should be delayed until the age of 12 months because spontaneous canalization occurs in about 95% of cases. Probing performed within the first 2 years of life has a very high success rate, but thereafter the efficacy decreases. It should be carried out under a general anaesthetic and preferably through the upper punctum (Fig. 2.23). The rationale is to manually overcome the obstructive membrane at the Hasner valve. After probing, the lacrimal system is irrigated with saline labelled with fluorescein. If fluorescein can be recovered by aspiration from the pharynx, successful probing is confirmed. Postoperative antibiotic drops are used q.i.d. for 1 week. If, after 6 weeks, there is no improvement, probing should be repeated. Nasal endoscopic monitoring of probing is recommended, especially for repeated probing, to detect anatomical abnormalities and ensure correct probe position.

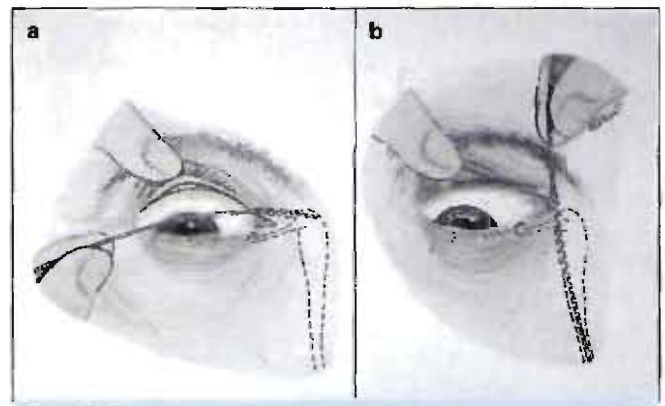

Fig. 2.23
Technique of probing of the nasolacrimal duct

4. Results. Ninety per cent of children are cured by the first probing and a further 6% by the second. Failure is usually the result of abnormal anatomy, which can usually be recognized by difficulty in passing the probe and subsequent non-patency of the lacrimal drainage system on irrigation. If symptoms persist despite two technically satisfactory probings, temporary intubation with fine silastic tubes or balloon dilatation of the nasolacrimal duct may effect a cure. Patients who fail to respond to such measures can be treated with DCR performed between the ages of 3 and 4 years, provided the obstruction is distal to the lacrimal sac.

Fig. 2.24
Amniontocele (Courtesy of R. Welham)

Congenital dacryocele

A congenital dacryocele (amniontocele) is a collection of amniotic fluid or mucus in the lacrimal sac caused by an imperforate Hasner valve.

1. **Presentation** is perinatal with a bluish cystic swelling at or below the medial canthal area, accompanied by epiphora (Fig. 2.24).
2. **Signs.** A tense lacrimal sac which is initially filled with mucus but may become secondarily infected.

> ***NB:*** It should not be mistaken for an encephalocele, which is characterized by a pulsatile swelling above the medial canthal tendon.

3. **Treatment** is initially conservative but if this fails probing should not be delayed.

Principles of lacrimal surgery

Conventional DCR

This is indicated for obstruction beyond the medial opening of the common canaliculus (i.e. the canalicular system is patent). In principle this operation involves anastomosing the lacrimal sac to the nasal mucosa of the middle nasal meatus. The procedure is performed under general hypotensive anaesthesia.

1. **Technique**
   a. The middle nasal mucosa is packed with sterile ribbon gauze soaked in 2% lignocaine with 1:200,000 adrenaline, to achieve vasoconstriction of the mucosa.
   b. A straight vertical incision is made 10 mm medial to the inner canthus, avoiding the angular vein (Fig. 2.25a).
   c. The anterior lacrimal crest is exposed by blunt dissection and the superficial portion of the medial palpebral ligament divided.
   d. The periosteum is divided from the spine on the anterior lacrimal crest to the fundus of the sac and reflected forwards. The sac is reflected laterally from the lacrimal fossa (Fig. 2.25b).
   e. The anterior lacrimal crest and the bone from the lacrimal fossa are removed (Fig. 2.25c).
   f. A probe is introduced into the lacrimal sac through the lower canaliculus and the sac is incised in an 'H-shaped' manner to create two flaps.
   g. A vertical incision is made in the nasal mucosa to create anterior and posterior flaps (Fig. 2.25d).
   h. The posterior flaps are sutured (Fig. 2.25e).
   i. The anterior flaps are sutured (Fig. 2.25f).
   j. The medial canthal tendon is resutured to the periosteum and the skin incision closed with interrupted sutures.
2. **Results** in experienced hands are excellent with a success rate of over 90%.
3. **Causes of failure** include inadequate size and position of the ostium, unrecognized common canalicular obstruction, scarring and the 'stump syndrome', in which the surgical opening in the lacrimal bone is too small and too high. There is thus a dilated lacrimal sac lateral to and below the level of the inferior margin of the ostium, in which secretions collect, unable to gain access to the ostium and thence the nasal cavity.
4. **Potential complications** include cutaneous scarring, injury to medial canthal structures, haemorrhage, cellulitis and cerebrospinal fluid rhinorrhoea, if the subarachnoid space is inadvertently entered.

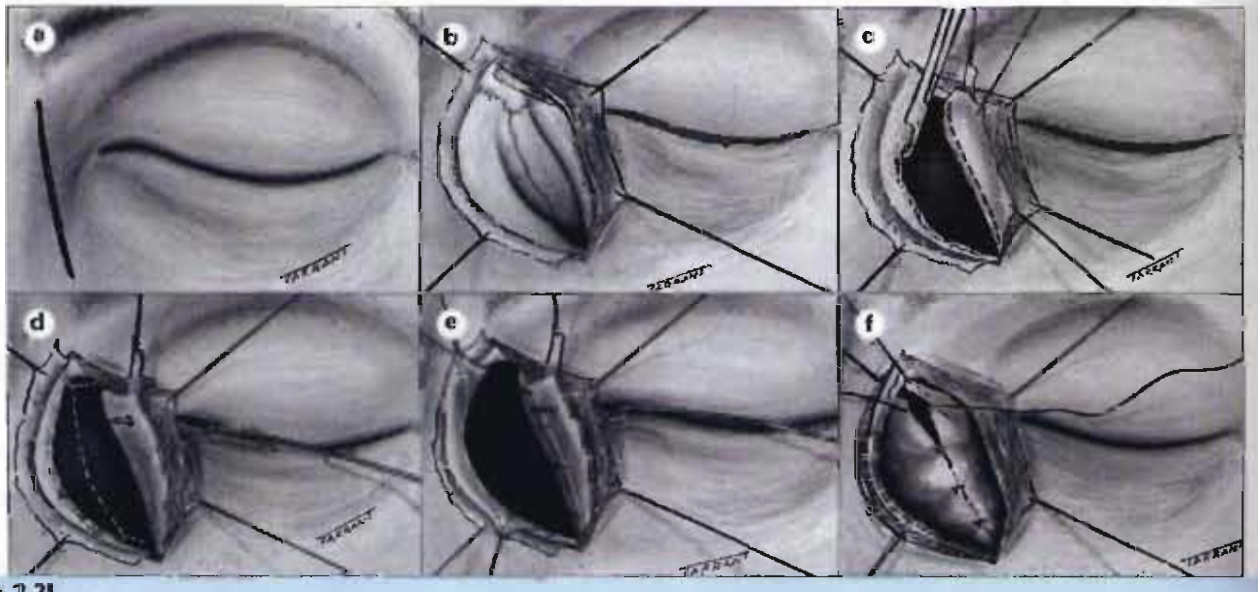

Fig. 2.25
Technique of dacryocystorhinostomy (see text)

Endoscopic DCR

This may be considered for obstruction beyond the medial opening of the common canaliculus, particularly following failed conventional DCR. The procedure can be performed either under general anaesthesia (without hypotension) or local anaesthesia. Advantages over conventional DCR include the lack of skin incision, shorter operating time, lower risk of interfering with the physiological lacrimal pump mechanism, minimal blood loss and no risk of cerebrospinal fluid rhinorrhoea.

1. **Technique.** A slender light pipe is passed through the lacrimal puncta and canaliculi into the lacrimal sac and viewed from within the nasal cavity with an endoscope. The remainder of the procedure is performed from within the nasal cavity.
   a. The mucosa over the frontal process of the maxilla is stripped.
   b. A part of the nasal process of the maxilla is removed.
   c. The lacrimal bone is broken off piecemeal.
   d. The lacrimal sac is opened.
   e. Silicone tubes are passed through the upper and lower puncta, pulled out through the ostium and tied within the nose.
2. **Results.** The success rate is about 85%.

Endolaser DCR

Performed with a holmium:YAG laser, this is a quick procedure which can be carried out under local anaesthesia. It is therefore particularly suitable for elderly patients. The success rate is only about 70% but because normal anatomy is not disrupted it does not prejudice subsequent surgical intervention in the cases that fail.

Lester Jones tube

Insertion of a Lester Jones tube is indicated when there is absence of canalicular function, either due to obstruction less than 8 mm from the puncta, or due to lacrimal pump failure.

a. A DCR is performed as far as suturing the posterior flaps.
b. The caruncle is partially excised.
c. A stab incision is made with a Graefe knife from a point about 2 mm behind the inner canthus (under the former caruncle) in a medial direction, so that the tip of the knife emerges just behind the anterior flap of the lacrimal sac (Fig. 2.26a).
d. The tract is enlarged sufficiently with a microtrephine to allow the introduction of a polythene tube (Fig. 2.26b).
e. The incision is sutured as for a DCR.
f. After 2 weeks the polythene tube is replaced by a glass tube.

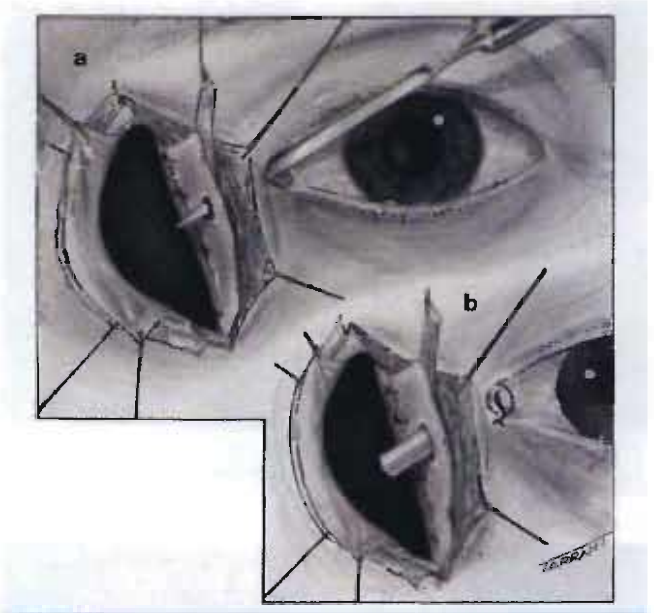

Fig. 2.26
Technique of Lester Jones tube insertion (see text)

Balloon dacryocystoplasty

This may be a satisfactory primary treatment for adults with partial nasolacrimal duct obstruction who do not exhibit signs of chronic infection.

Infections of lacrimal passages

Chronic canaliculitis

Chronic canaliculitis is an uncommon condition, frequently caused by *Actinomyces*, which are anaerobic Gram-positive bacteria. While a diverticulum or obstruction of the canaliculus can promote anaerobic bacterial growth secondary to stasis, in most cases there is no identifiable predisposition.

1. **Presentation** is with unilateral epiphora associated with chronic mucopurulent conjunctivitis, refractory to conventional treatment.
2. **Signs**
   - Pericanalicular inflammation is characterized by oedema of the canaliculus (Fig. 2.27) and a 'pouting' punctum best seen with the slit-lamp (Fig. 2.28).
   - Concretions consisting of sulphur granules are expressed on canalicular compression with a glass rod (Fig. 2.29).

> ***NB:*** In contrast to dacryocystitis, there is no nasolacrimal duct obstruction, lacrimal sac distension or inflammation.

3. **Treatment**
   a. Topical antibiotics such as ciprofloxacin q.i.d. for 10 days may be tried initially but are rarely curative.

Fig. 2.27
Oedema of the left upper canaliculus in chronic canaliculitis

Fig. 2.28
Pouting of the punctum in chronic canaliculitis

Fig. 2.29
Expressed concretions in chronic canaliculitis

b. Canaliculotomy (Fig. 2.30) involving a linear incision into the conjunctival side of the canaliculus is the most effective treatment, although occasionally it may result in scarring and interference with canalicular function.

Fig. 2.30
Exposure of large concretions following canaliculotomy in chronic canaliculitis

Dacryocystitis

Infection of the lacrimal sac is usually secondary to obstruction of the nasolacrimal duct. It may be acute or chronic and is most commonly caused by staphylococci.

Acute dacryocystitis

1. **Presentation** is with subacute onset of pain, redness and swelling at the medial canthus and epiphora.

Fig. 2.31
Acute dacryocystitis

2. **Signs.** A very tender, red, tense swelling at the medial canthus which may be associated with preseptal cellulitis in severe cases (Fig. 2.31).
3. **Treatment**
   a. ***Initial*** treatment involves the application of local warmth and oral antibiotics such as flucloxacillin.

> *NB:* Irrigation and probing should not be performed.

   b. ***Incision and drainage.*** The infection may sometimes extend outside the sac to produce an abscess in the periorbital soft tissue (lacrimal abscess). If pus points and the abscess threatens to drain spontaneously (Fig. 2.32), incision and drainage may be considered. This, however, carries a risk of the development of a lacrimal fistula, which may serve as a conduit for tears from the lumen of the lacrimal sac to the skin surface.
   c. *DCR* is usually necessary after the acute infection has been controlled and should not be delayed because of the risk of recurrent infection.

Fig. 2.32
Lacrimal sac abscess

Fig. 2.33
Mucocele

Chronic dacryocystitis

1. **Presentation** is with epiphora which may be associated with a chronic or recurrent unilateral conjunctivitis.
2. **Signs.** A painless swelling at the inner canthus caused by a mucocele (Fig. 2.33). Obvious swelling may be absent, although pressure over the sac commonly still results in reflux of mucopurulent material through the canaliculi (*see* Fig. 2.10).

> *NB:* It is often wise to postpone intraocular surgery until lacrimal infection has been treated, owing to the grave risk of endophthalmitis.

3. **Treatment** is with DCR.

CHAPTER 3

The Dry Eye

Applied physiology 57
Causes 57
Clinical features 58
Special investigations 59
Treatment 60

Applied physiology

The main lacrimal glands produce about 95% of the aqueous component of tears and the accessory lacrimal glands of Krause and Wolfring produce the remainder. Secretion of tears has basic (resting) and much greater reflex components. Reflex secretion occurs in response to corneal and conjunctival sensory stimulation, tear break-up and dry spot formation or ocular inflammation. It is reduced by topical anaesthesia. Although in the past basic secretion was ascribed to the accessory lacrimal glands and reflex secretion to the main lacrimal glands, it is now thought that the whole mass of lacrimal tissue responds as one unit. The precorneal tear film consists of three layers: (a) *lipid*, (b) *aqueous* and (c) *mucin*, each of which has separate functions (Fig. 3.1).

Outer lipid layer

This is secreted by the meibomian glands.

1. **Functions**
   - To retard evaporation of the aqueous layer of the tear film.
   - To lower surface tension of the tear film. This, in turn, draws water into the tear film and thickens the aqueous layer.
   - To lubricate the eyelids as they pass over the surface of the globe.
2. **Dysfunction** of this layer may result in an *evaporative dry eye*.

Middle aqueous layer

This is secreted by the lacrimal glands and consists of proteins, electrolytes and water.

1. **Functions**
   - To supply atmospheric oxygen to the avascular corneal epithelium.
   - Antibacterial function due to the presence of tear proteins such as IgA, lysozyme and lactoferrin.
   - To abolish any minute irregularities of the anterior corneal surface.
   - To wash away debris and noxious stimuli and allow the passage of leucocytes after injury.
2. **Deficiency** of this layer results in a *hyposecretive dry eye*.

Inner mucin layer

This is secreted by the conjunctival goblet cells, the crypts of Henle and the glands of Manz.

1. **Function**
   - Wetting of the cornea by converting the corneal epithelium from a hydrophobic to a hydrophilic surface (Fig. 3.2, right).
   - Lubrication.
2. **Deficiency** of this layer may be a feature of both hyposecretive and evaporative states (Fig. 3.2, left).

The tear film is mechanically spread over the ocular surface through a neuronally controlled blinking mechanism and after a period of time is cleared through the nasolacrimal drainage system. The three factors required for effective resurfacing of the tear film are: (a) *normal blink reflex*, (b) *congruity between the external ocular surface and eyelids* and (c) *normal corneal epithelium*.

Causes

The terms 'dry eye' and 'keratoconjunctivitis sicca' (KCS) are synonymous. The two main categories are: (a) *hyposecretive*, which may be Sjögren or non-Sjögren, and (b) *evaporative*, although the two are not mutually exclusive.

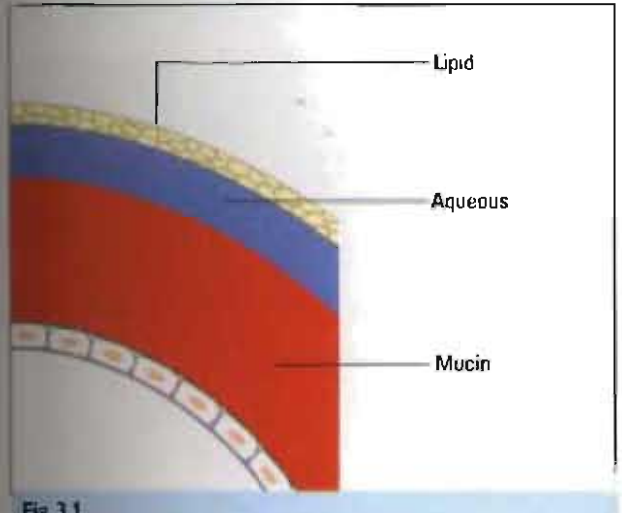

Fig. 3.1
The three layers of the precorneal tear film

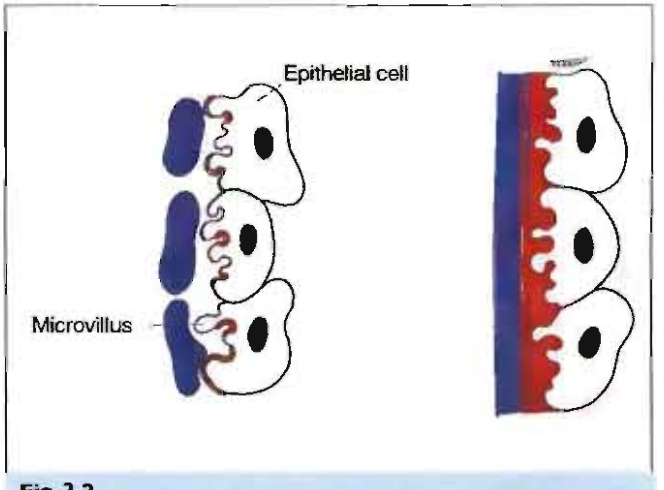

Fig. 3.2
Function of the mucin layer. **(Left)** in mucin deficiency, the aqueous layer (blue) cannot wet the corneal epithelium; **(right)** a normal amount of mucin (red) enables wetting of the corneal epithelium by the aqueous layer

Sjögren hyposecretive KCS

Sjögren syndrome is a cytokine and receptor-mediated inflammatory process that affects the lacrimal gland acini and ducts, leading to abnormalities in the tear film with resultant ocular surface disease.

1. **Primary Sjögren syndrome** is characterized by a dry mouth (xerostomia) and the presence of antibodies indicative of autoimmune pathogenesis.
2. **Secondary Sjögren** is characterized by a systemic autoimmune connective tissue disorder such as rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, dermatomyositis and polymyositis, mixed connective tissue disease, relapsing polychondritis or primary biliary cirrhosis, in addition to the features of primary Sjögren syndrome.

Non-Sjögren KCS

1. **Primary age-related** is the most common.
2. **Destruction of lacrimal tissue** by tumour or inflammation (e.g. pseudotumour, thyroid eye disease and sarcoidosis).
3. **Absence of the lacrimal gland** following surgical removal; rarely congenital.
4. **Obstruction of ductules** of the lacrimal gland as a result of severe conjunctival scarring (e.g. cicatricial pemphigoid and trachoma).
5. **Neurological lesions** such as familial dysautonomia (Riley–Day syndrome).

Evaporative KCS

1. **Oil deficiency** is most frequently secondary to obstructive meibomian gland dysfunction (*see* Chapter 1).
2. **Defective resurfacing** of the eye by the tear film as a result of abnormal lid–globe congruity or defective blinking.

Clinical features

Symptoms

The most common are irritation, foreign body sensation, burning, a stringy mucus discharge and transient blurring of vision. Less frequent symptoms include itching, photophobia and a tired or heavy feeling. Patients with filamentary keratitis (*see* below) may complain of severe pain brought on by blinking. Surprisingly, patients seldom complain that their eyes are dry, although some may report a lack of emotional tears or a deficient response when peeling onions. The symptoms of KCS are frequently exacerbated on exposure to conditions associated with increased tear evaporation (e.g. air-conditioning, wind, central heating) or prolonged reading, when blink frequency is reduced. Symptoms may be improved by lid closure.

Tear film abnormalities

1. **Mucus strands and debris** are an early sign. In the normal eye, as the tear film breaks down, the mucin layer becomes contaminated with lipid but is washed away. In the dry eye, the lipid-contaminated mucin accumulates in the tear film and tends to move with each blink. Mucin also has the interesting property of drying very quickly and rehydrating very slowly.
2. **The marginal tear meniscus** is a crude measure of the volume of aqueous in the tear film. The normal meniscus varies in height between 0.1 and 0.5 mm and forms a convex band with a regular upper edge. In KCS the tear meniscus becomes concave, irregular, thin (Fig. 3.3) or absent.
3. **Froth** in the tear film or along the eyelid margin occurs in meibomian gland dysfunction (*see* Fig. 1.33).

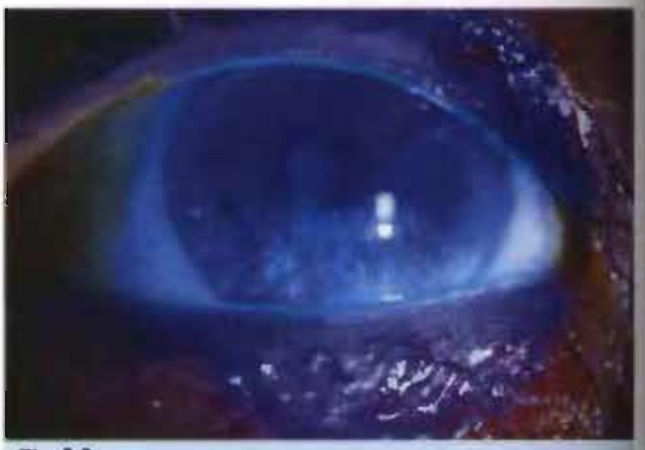

Fig. 3.3
Inferior punctate epithelial erosions stained with fluorescein and a thin marginal tear meniscus in keratoconjunctivitis sicca

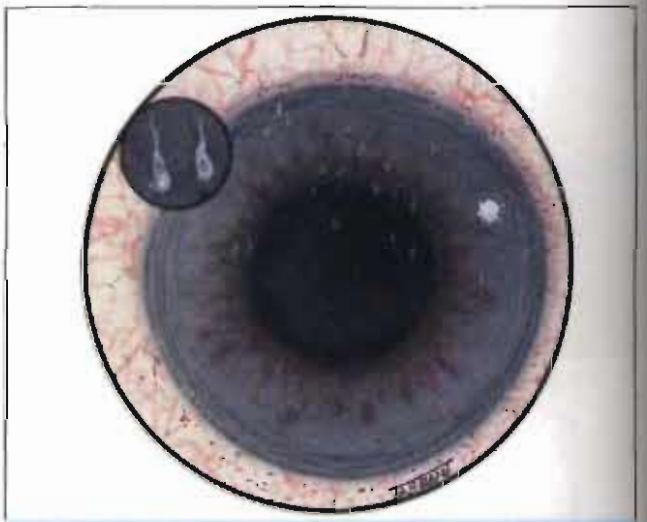

Fig. 3.4
Corneal filaments

Keratopathy

1. **Punctate epithelial erosions** involve the inferior cornea (see Fig. 3.3).
2. **Filaments** consist of small, comma-shaped mucus strands lined with epithelium attached at one end to the corneal surface (Fig. 3.4); the unattached end moves with each blink.
3. **Mucus plaques** consist of semi-transparent, white-to-grey, slightly elevated lesions of various sizes and shapes. They are composed of mucus, epithelial cells and proteinaceous and lipoidal material. They are usually seen in association with corneal filaments and both stain with rose bengal (Fig. 3.5).

NB: It should be remembered that a dry eye predisposes to bacterial keratitis and sterile ulceration, which may lead to perforation (Fig. 3.6).

Special investigations

Tear film break-up time

The tear film break-up time (BUT) is an index of precorneal tear film stability. It is measured as follows:

Fig. 3.5
Mucus plaques and a few filaments stained with rose bengal

Fig. 3.7
A dry spot caused by tear film break-up

a. Fluorescein is instilled into the lower fornix.
b. The patient is asked to blink several times and then stop.
c. The tear film is examined with a broad beam and a cobalt blue filter. After an interval of time, black spots or lines indicating the formation of dry areas will appear (Fig. 3.7).

The BUT is the interval between the last blink and the appearance of the first randomly distributed dry spot. The development of dry spots always in the same location should be ignored because this is caused by a local corneal surface abnormality and not by intrinsic instability of the tear film. A BUT of less than 10 seconds is abnormal.

Rose bengal

This dye has an affinity for dead or devitalized epithelial cells and mucus. It stains the exposed bulbar conjunctiva, resulting in the typical staining pattern of two triangles with their bases at the limbus (Figs 3.8 and 3.9). Corneal filaments and plaques are also shown up more clearly by the dye. One disadvantage of rose bengal is that it may cause ocular

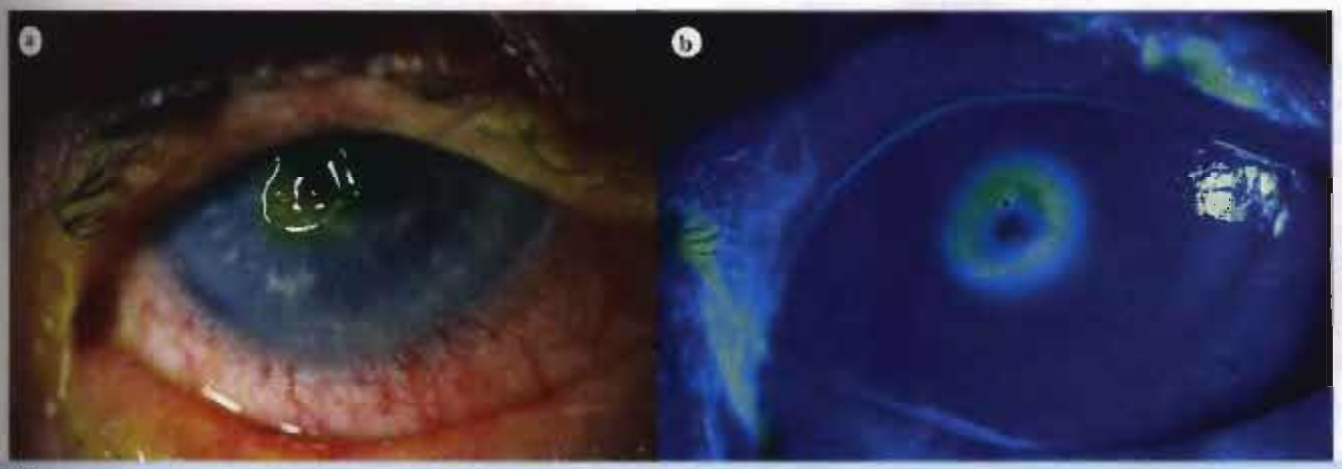

Fig. 3.6
(a) Corneal perforation in severe keratoconjunctivitis sicca; (b) same eye stained with fluorescein

Fig. 3.8
Mild staining with rose bengal

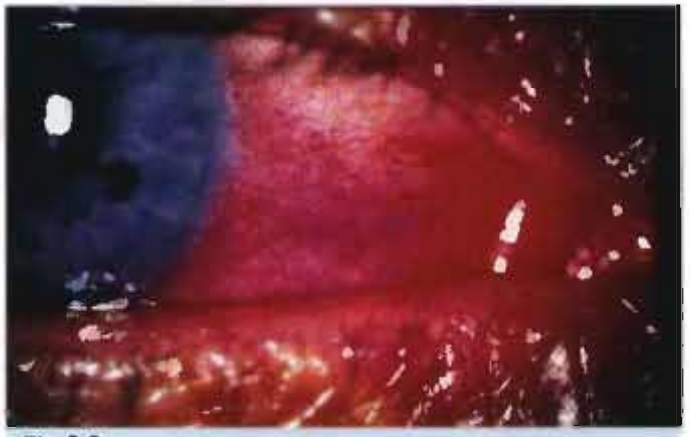

Fig. 3.9
Extensive staining with rose bengal

irritation which can last for up to a day, particularly in severely dry eyes. To minimize irritation a very small drop should be used, but a topical anaesthetic should not be used before instillation because it may induce a false-positive result.

Schirmer test

This is useful when aqueous deficiency is suspected in the absence of slit-lamp signs of KCS. The test involves measuring the amount of wetting of a special (no. 41 Whatman) filter paper, 5 mm wide and 35 mm long. The test can be performed with or without topical anaesthesia. In theory, when performed without an anaesthetic (Schirmer 1) it measures total secretion, basic and reflex, whereas with an anaesthetic (Schirmer 2) it measures only basic secretion. In practice, however, topical anaesthesia reduces reflex secretion but does not abolish it completely. The test is performed as follows:

a. The eye is gently dried.

b. The filter paper is folded 5 mm from one end and inserted at the junction of the middle and outer third of the lower lid, taking care not to touch the cornea.

Fig. 3.10
Schirmer test

c. The patient is asked to keep the eyes open and to blink normally (Fig. 3.10).
d. After 5 minutes the filter paper is removed and the amount of wetting measured.

A normal result is over 15 mm without anaesthesia and slightly less with anaesthesia. Between 6 and 10 mm is borderline and less than 6 mm indicates impaired secretion.

Treatment

The main aims of treatment of KCS are to relieve discomfort, provide a smooth optical surface and prevent structural corneal damage. One or more of the following measures may be used simultaneously.

Preservation of existing tears

1. **Reduction of room temperature**, by avoiding central heating, to minimize evaporation of tears.
2. **Room humidifiers** may be tried but are frequently disappointing because the apparatus is incapable of significantly increasing the relative humidity of an average-sized room. A temporary local increase in humidity can be achieved with moist chamber goggles.
3. **A small lateral tarsorrhaphy** which decreases the surface area of the interpalpebral fissure may be helpful.

Tear substitutes

1. **Drops**
   - Hypromellose (Isopto Plain, Isopto Alkaline, Tears Naturale).
   - Polyvinyl alcohol (Hypotears, Liquifilm Tears, Snotears).
   - Sodium hyaluronate (VISMED, VISLUBE).

- Sodium chloride (Normasol, Steripod Blue).
- Povidone (Oculotet).

NB: The main disadvantages of drops are short duration of action and the development of sensitivity to the preservative (e.g. benzalkonium chloride, thiomersal). The latter can be avoided by using a preservative-free preparation (Minims).

2. **Gels** (Viscotears, Gel Tears) consist of carbomers. In general, they are preferable to drops because they are instilled less frequently.
3. **Ointments** containing petrolatum mineral oil (Lacri-Lube, Lubri-Tears) can be used at bedtime.

Mucolytic agents

Acetylcysteine 5% drops (Ilube) may be useful in patients with corneal filaments and mucous plaques. They are used q.i.d. and may cause irritation following instillation. Acetylcysteine is also malodorous and has a limited bottle life, so that it can only be used for up to 2 weeks.

Reduction of tear drainage

Punctal occlusion preserves natural tears and prolongs the effect of artificial tears. It is of greatest value in patients with severe KCS, particularly when associated with toxicity from preservatives.

1. **Temporary occlusion** of the puncta can be achieved by inserting commercially available collagen plugs into the canaliculi. The main aim of temporary occlusion is to ensure that epiphora does not occur following permanent occlusion. Initially all four puncta are occluded and the patient is reviewed after 1 week. If epiphora is induced, the upper plugs are removed and the patient is re-examined 1 week later. If the patient is now asymptomatic, the plugs are removed and the inferior canaliculi are permanently occluded. Temporary occlusion can also be performed with the argon laser.
2. **Reversible long-term occlusion** lasting several months can be achieved with silicone plugs. Potential problems include extrusion, granuloma formation and distal migration causing inflammation.

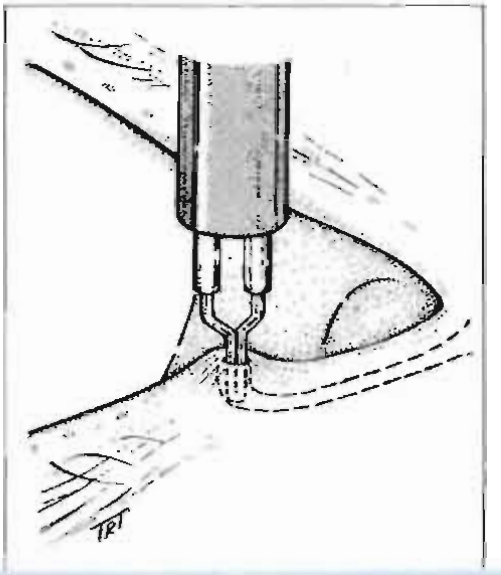

Fig. 3.11
Permanent punctal occlusion

3. **Permanent occlusion** should be undertaken only in patients with severe KCS and repeated Schirmer test values of 2 mm or less. It should not be performed in patients who develop epiphora following temporary occlusion of only the inferior puncta. Permanent occlusion should also be avoided in young patients as their tear production tends to fluctuate. Permanent occlusion is achieved by vigorous punctal dilatation followed by heating for 1 second the mucosal lining of the proximal canaliculus with gentle cautery (Fig. 3.11). Following successful punctal occlusion, it is important to watch for signs of recanalization. It is also important to treat any associated disorder such as chronic blepharitis and superinfection before occlusion.

Other options

1. **Topical cyclosporin** (0.05%, 0.1%) is a safe, well-tolerated and effective new medication which reduces cell-mediated inflammation of lacrimal tissue.
2. **Oral cholinergic agents** such as pilocarpine (Salagan) are very effective in the relief of xerostomia and about 40% of KCS patients also obtain relief.

CHAPTER 4

Conjunctiva

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Introduction

Applied anatomy

Subdivisions

1. **Palpebral** starts at the mucocutaneous junction of the lid margins and is firmly adherent to the tarsal plates.
2. **Forniceal** is loose and redundant so that it swells easily and may be thrown into folds.
3. **Bulbar** covers the anterior sclera. The stroma of the bulbar conjunctiva is loosely attached to the underlying Tenon capsule, except at the limbus, where the attachment is firm.

Histology

1. **The conjunctival epithelium** is between two and five cell layers thick. Basal cuboidal cells evolve into flattened polyhedral cells as they reach the surface. With chronic exposure and drying, the epithelium may become keratinized.
2. **The stroma** (substantia propria) consists of richly vascularized connective tissue, separated from the epithelium by a basement membrane. The adenoid superficial layer does not develop until about 3 months after birth, hence the inability of the newborn to produce a follicular conjunctival reaction. The deep, thicker fibrous layer is continuous with the tarsal plates and belongs to the subconjunctival tissues rather than the conjunctiva.

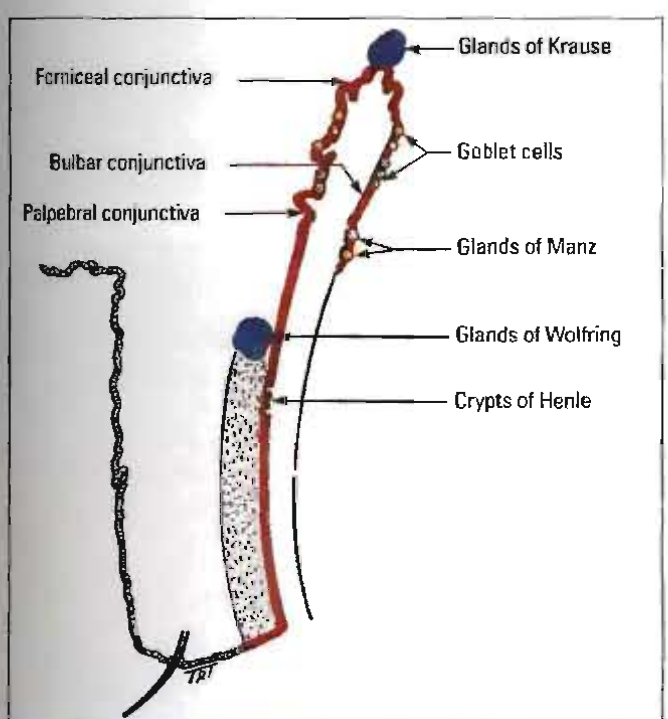

Fig. 4.1
Anatomy of the conjunctiva and its glands

Glands

1. **Mucin secretors** (Fig. 4.1)
   a. *Goblet cells*, located within the epithelium, are most dense inferonasally.
   b. *Crypts of Henle* are located along the upper third of the superior tarsal conjunctiva and along the lower third of the inferior tarsal conjunctiva.
   c. *Glands of Manz* encircle the limbus.

> ***NB:*** Destructive disorders of the conjunctiva such as cicatricial pemphigoid frequently damage the mucin secretors, whereas chronic inflammatory disorders may be associated with an increase in number of goblet cells.

2. **Accessory lacrimal glands** of Krause and Wolfring are located deep within the substantia propria.

Clinical evaluation

Clinical features relevant to the differential diagnosis of conjunctival inflammation are: (a) *symptoms*, (b) *discharge*, (c) *conjunctival reaction*, (d) *membranes* and (e) *lymphadenopathy*.

Symptoms

1. **Non-specific** symptoms include lacrimation, irritation, stinging, burning and photophobia.
2. **Pain** and foreign body sensation suggest associated corneal involvement.
3. **Itching** is the hallmark of allergic conjunctivitis although it may also occur in blepharitis and keratoconjunctivitis sicca.

Discharge

This is composed of the exudate that has filtered through the conjunctival epithelium from dilated blood vessels. On the surface of the conjunctiva, variable amounts of epithelial debris, mucus and tears are added. The discharge can range from watery through mucopurulent to grossly purulent.

1. **A watery** discharge is composed of a serous exudate and a variable amount of reflexly secreted tears. It is typical of acute viral and acute allergic inflammations.
2. **A mucoid** discharge is typical of vernal conjunctivitis and keratoconjunctivitis sicca.
3. **A purulent** discharge occurs in severe acute bacterial infections.
4. **A mucopurulent** discharge occurs in mild bacterial as well as chlamydial infections.

Conjunctival reaction

1. **Conjunctival injection** is frequently maximal in the fornices. A velvety, beefy-red conjunctiva suggests a bacterial aetiology (Fig. 4.2).
2. **Subconjunctival haemorrhages** usually occur with viral infections although they may be present with bacterial infections with *Strep. pneumoniae* and *H. aegypticus* (Fig. 4.3).

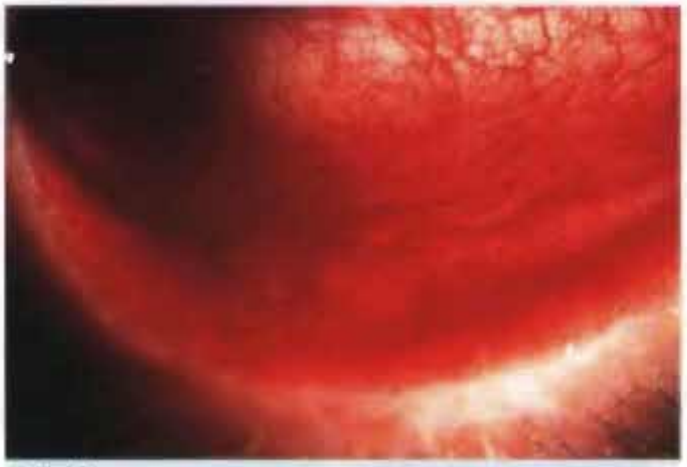

Fig. 4.2
Conjunctival injection in bacterial infection

Fig. 4.5
Conjunctival scarring

Fig. 4.3
Subconjunctival haemorrhage

Fig. 4.6
Conjunctival follicles

Fig. 4.4
Severe chemosis

3. **Oedema** (chemosis) may occur when the conjunctiva is severely inflamed. Exudation of protein-rich fluid through the walls of the inflamed blood vessels produces a translucent swelling. Large redundant folds may form in the fornices (Fig. 4.4) and in severe cases chemotic conjunctiva may protrude through the closed eyelids.
4. **Scarring** may indicate trachoma, ocular cicatricial pemphigoid, atopic conjunctivitis or the prolonged use of topical medication (Fig. 4.5).
5. **Follicular reaction**
   a. ***Composition.*** Follicles are subepithelial foci of hyperplastic lymphoid tissue within the stroma associated with accessory vascularization.
   b. ***Signs*** (Fig. 4.6)
      - Multiple, discrete, slightly elevated lesions reminiscent of small grains of rice, most prominent in the fornices.
      - Each follicle is encircled by a tiny blood vessel and the size of each lesion, which can vary from 0.5 to 5 mm, is related to the severity and duration of the inflammation.
      - As the follicle increases in size, the accompanying vessels are displaced peripherally, eventually appearing as a vascular capsule enclosing the base of the follicle.

c. ***Causes*** include viral and chlamydial infections, Parinaud oculoglandular syndrome and hypersensitivity to topical medication.

> ***NB:*** Asymptomatic follicles in children (folliculosis) have no clinical significance.

6. **Papillary reaction** is non-specific and therefore of less diagnostic value than a follicular response.
   a. ***Composition***
      - Hyperplastic conjunctival epithelium thrown into numerous folds or projections, with central vessels and a diffuse infiltrate of chronic inflammatory cells, including lymphocytes, plasma cells and eosinophils.
      - Papillae can develop only in the palpebral conjunctiva and the bulbar conjunctiva at the limbus, where the conjunctival epithelium is attached to the underlying structures by fibrous septa.
   b. ***Signs*** (Fig. 4.7)
      - Papillae are most frequently seen in the upper palpebral conjunctiva as a fine mosaic-like pattern of elevated polygonal hyperaemic areas separated by paler channels.
      - The central fibrovascular core produces a glomerulus-like appearance on reaching the surface.
      - With prolonged inflammation, the fibrous septa which anchor the papillae to the underlying tissues may rupture, leading to confluence and increase in size.
      - Late changes include superficial stromal hyalinization and formation of crypts containing goblet cells between the papillae.

Fig. 4.7
Conjunctival papillae (Courtesy of C. Barry)

Fig. 4.8
Normal appearance of the medial aspect of the upper palpebral conjunctiva

> ***NB:*** The appearance of the normal superior edge of the tarsal plate (inferior when everted) may mimic papillae and follicles and should therefore not be used as a clinical sign (Fig. 4.8).

   c. ***Causes*** include chronic blepharitis, allergic and bacterial conjunctivitis, contact lens wear, superior limbic keratoconjunctivitis and floppy eyelid syndrome.

Membranes

1. **Pseudomembranes** consist of coagulated exudate adherent to the inflamed conjunctival epithelium. Characteristically, they can be easily peeled off, leaving the epithelium intact (Fig. 4.9). Causes include severe adenoviral and gonococcal infection, ligneous conjunctivitis and Stevens–Johnson syndrome.
2. **True membranes** infiltrate the superficial layers of the conjunctival epithelium. Attempts to remove the membrane may be accompanied by tearing of the epithelium and bleeding. The main causes are infections resulting from *Strep. pyogenes* and diphtheria.

Lymphadenopathy

Lymphatic drainage of the conjunctiva is to the preauricular and submandibular nodes, which corresponds to the drainage of the eyelids (*see* Fig. 1.3). The main causes of lymphadenopathy are viral, chlamydial and gonococcal infections and Parinaud oculoglandular syndrome.

Fig. 4.9
Removal of a conjunctival pseudomembrane (Courtesy of J. Dart)

Laboratory investigations

Indications

1. **Severe purulent conjunctivitis**: to identify pathogens and institute appropriate antimicrobial therapy based on sensitivity.
2. **Follicular conjunctivitis**: to differentiate viral from early chlamydial infection.
3. **Conjunctival inflammations**, in which the clinical picture is insufficiently distinctive to suggest an aetiological diagnosis.
4. **Neonatal conjunctivitis.**

Specific investigations

1. **Cultures** are now rarely performed as they have been replaced by more accurate and quicker techniques.
2. **Cytological investigation**, based on the presence of characteristic cellular infiltrates, is insensitive and subjective.
3. **Inoculation** of susceptible cell lines and observation of cytopathic effect or visualization with various chemical and immunological staining techniques.
4. **Detection of viral or chlamydial antigens** in conjunctival and corneal specimens.
5. **Impression cytology** in which a piece of cellulose acetate filter paper is pressed against the conjunctiva or cornea. Surface epithelial cells adhere to the paper when removed and can be examined microscopically. This may be useful in the diagnosis of ocular surface neoplasia, dry eyes, ocular cicatricial pemphigoid, limbal stem cell failure and infections.
6. **Polymerase chain reaction** (PCR) allows the speedy identification of extremely small quantities of DNA with a very high degree of specificity. It is useful for the detection of adenovirus, herpes simplex and *Chlamydia trachomatis* in conjunctival swabs.

Bacterial infections

Simple bacterial conjunctivitis

Simple bacterial conjunctivitis is a common and usually self-limiting condition which most commonly affects children. The most frequent causative organisms are *Staph. epidermidis*, *Staph. aureus*, *Strep. pneumoniae* and *H. influenzae*. Spread of the infection is usually the result of direct contact with infected secretions.

Clinical features

1. **Presentation** is with acute redness, grittiness, burning and discharge. On waking, the eyelids are frequently stuck together and difficult to open as a result of the accumulation of exudate during the night. Both eyes are usually involved, although one may become affected before the other by a day or so.
2. **Signs**
   - The eyelids are crusted and may be oedematous (Fig. 4.10).
   - The discharge is initially watery (Fig. 4.11), mimicking viral conjunctivitis, but within a day or so it becomes mucopurulent (Fig. 4.12). Mucous strands may develop in the inferior fornix.
   - Injection is maximal in the fornices and least at the limbus.
   - The tarsal conjunctiva has a velvety, beefy-red appearance and shows mild papillary changes.
   - Superficial punctate epithelial erosions are frequent but innocuous.

Treatment

Even without treatment, simple conjunctivitis usually resolves within 10–14 days and laboratory tests are not routinely performed. Before initiating treatment, it is

Fig. 4.10
Severe crusting of the eyelids in bacterial conjunctivitis

Fig. 4.11
Watery discharge

Fig. 4.12
Mucopurulent discharge in bacterial conjunctivitis

important to clean the eyelids and lashes of discharge. Broad-spectrum antibiotics should be administered in drop form during waking hours and as ointment at bedtime until the discharge has ceased.

1. **Antibiotic drops**
   a. ***Fusidic acid*** (Fucithalmic) is a viscous suspension which is useful for staphylococcal infections but not for most Gram-negative bacteria. Initial treatment is q.i.d. for 48 hours and then b.d.
   b. ***Chloramphenicol*** has a broad spectrum and is initially administered every 1–2 hours.
   c. ***Other antibiotics*** in drop form currently available include: ciprofloxacin, ofloxacin, lomefloxacin, gentamicin, neomycin, framycetin, tobramycin, Neosporin (polymyxin B + neomycin + gramicidin) and Polytrim (polymyxin + trimethoprim).
2. **Antibiotic ointments** provide higher concentrations for longer periods than drops, but use during the day is limited because they cause blurred vision. However, ointments can be used at night to provide a good concentration of antibiotic during sleep. Antibiotics available in ointment form include chloramphenicol, gentamicin, tetracycline, framycetin, Polyfax (polymyxin B + bacitracin) and Polytrim.

Gonococcal keratoconjunctivitis

Gonorrhoea is a venereal genitourinary tract infection caused by the Gram-negative diplococcus *Neisseria gonorrhoeae*, which is capable of invading the intact corneal epithelium.

Conjunctivitis

1. **Presentation** is with acute conjunctival discharge.
2. **Signs**
   - The eyelids are oedematous and tender.
   - The discharge is profuse and purulent (Fig. 4.13).
   - Intense conjunctival hyperaemia, chemosis and frequently pseudomembrane formation (Fig. 4.14).
   - Lymphadenopathy is prominent and, in severe cases, suppuration may occur.

Fig. 4.13
Purulent discharge in gonococcal conjunctivitis

Fig. 4.14
Conjunctival pseudomembranes

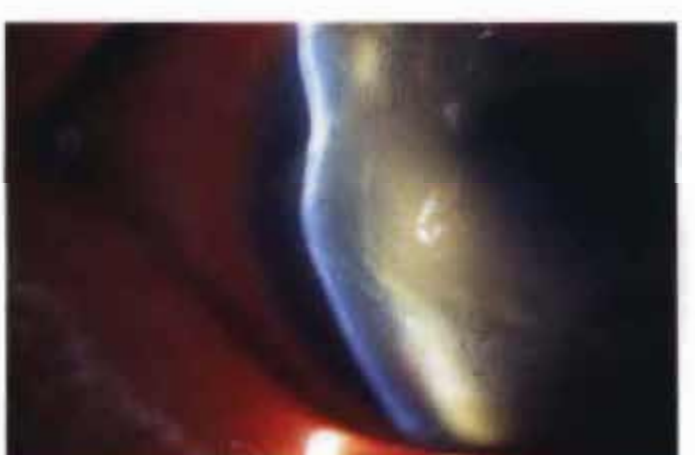

Fig. 4.15
Corneal ulceration in gonococcal infection

Fig. 4.16
Corneal perforation and endophthalmitis in gonococcal infection

Keratitis

Unless conjunctivitis is treated promptly keratitis may occur and progress as follows:

- Marginal ulceration in the pus filled sulcus between the chemosed conjunctiva and the cornea at the limbus.
- Coalescence to form a peripheral ring ulcer.
- Central ulceration (Fig. 4.15) which may rapidly lead to perforation and endophthalmitis (Fig. 4.16).

Treatment

The patient should be hospitalized, cultures taken and the discharge removed at frequent intervals.

1. **Systemic** treatment is with cefotaxime 1 g intravenously b.d. If only the conjunctiva is involved 1 day's treatment may suffice, but corneal involvement may necessitate treatment for longer.
2. **Topical** gentamicin or bacitracin initially at very frequent intervals.

NB: It is important to recognize and treat any associated chlamydial infection.

Viral infections

Adenoviral keratoconjunctivitis

The spectrum of adenoviral eye infection varies from mild and almost inapparent disease to full-blown infection with significant morbidity. It is an occupational hazard of ophthalmologists. Transmission of this highly contagious virus is via respiratory or ocular secretions, and dissemination is by contaminated towels or equipment such as tonometer heads. The incubation period is 4–10 days. Following the onset of conjunctivitis the virus is shed for about 12 days. Precautions must be taken to avoid transmission following examination of patients with suspected adenovirus infection. Thorough washing of hands is most important, as is meticulous disinfection of ophthalmic instruments. In addition, infected hospital personnel should not come in contact with patients.

Causative viruses

1. **Pharyngoconjunctival fever (PCF)** is most frequently caused by adenovirus types 3, 4 and 7 and occasionally type 5. It is transmitted by droplets and typically affects children who also develop an upper respiratory tract infection. Keratitis develops in about 30% of cases but is seldom severe.
2. **Epidemic keratoconjunctivitis (EKC)** is most frequently caused by adenovirus types 8 and 19, but several other types may also be responsible. The infection is transmitted by hand to eye contact, instruments and solutions. In contrast to PCF it does not cause systemic symptoms. Keratitis, which may be severe, develops in about 80% of cases.

Fig. 4.17
Eyelid oedema in adenoviral infection

Fig. 4.18
Conjunctival follicles in adenoviral infection

Conjunctivitis

1. **Presentation** is with acute watering, redness, discomfort and photophobia frequently involving both eyes.
2. **Signs**
   - Eyelid oedema (Fig. 4.17).
   - Watery discharge and conjunctival follicles (Fig. 4.18).
   - Subconjunctival haemorrhages, chemosis and pseudomembranes (Fig. 4.19) in severe cases.
   - Tender lymphadenopathy.
3. **Treatment** is largely symptomatic and supportive. Spontaneous resolution occurs within 2 weeks. Antiviral agents are ineffective and topical steroids should be avoided unless the inflammation is very severe.

Keratitis

1. **Signs**
   a. *Stage 1* occurs within 7–10 days of the onset of symptoms and is characterized by a punctate epithelial keratitis which resolves within 2 weeks (Fig. 4.20).
   b. *Stage 2* is characterized by focal, white, subepithelial opacities which develop beneath the fading epithelial lesions (Fig. 4.21). They are thought to represent immune response to the virus and may be associated with mild transient anterior uveitis.
   c. *Stage 3* is characterized by anterior stromal infiltrates which gradually fade over months or years (Fig. 4.22).
2. **Treatment** with topical steroids is indicated only if the eye is uncomfortable or visual acuity diminished by stage 3 lesions. Steroids do not shorten the natural course of the disease but merely suppress the corneal inflammation so that the lesions tend to recur if steroid therapy is discontinued prematurely.

Fig. 4.19
Conjunctival pseudomembranes in adenoviral infection

Fig. 4.20
Punctate epithelial keratitis in stage 1 adenoviral infection

Fig. 4.21
Subepithelial opacities in stage 2 adenoviral infection

Fig. 4.22
Anterior stromal opacities in stage 3 adenoviral infection

Molluscum contagiosum conjunctivitis

Molluscum is an oncogenic virus that produces characteristic lesions on the skin and, less commonly, on mucous membranes. Spread is by close contact. The condition typically affects adolescent children and young adults. Molluscum is also a common finding in patients with AIDS, in whom multiple lesions may develop. Patients with ocular involvement may also manifest mollusca involving other parts of the body.

Fig. 4.23
Follicular conjunctivitis associated with a solitary molluscum lesion on the lower lid margin

1. **Signs**
   - The lid margin shows a small, pale, waxy, umbilicated nodule.
   - The lesion may be missed if atypical in appearance or some distance from the lid margin.
   - The discharge is usually mild and mucoid.
   - The conjunctiva shows a follicular response ipsilateral to the lid lesion (Fig. 4.23).
   - Rarely, immunocompromised patients may develop molluscum nodules on the bulbar conjunctiva.
   - Long-standing cases may develop fine epithelial keratitis which may progress to pannus formation if untreated.
2. **Treatment** involves destruction of the lid lesion by expression, shave excision, cryotherapy or cauterization.

Chlamydial infections

Adult chlamydial conjunctivitis

Adult chlamydial conjunctivitis is a sexually transmitted disease caused by serotypes D to K *Chlamydia trachomatis*. Patients with chlamydial conjunctivitis are generally young and many have a concomitant genital infection (cervicitis in women and urethritis in men) which may be asymptomatic (see Chapter 20). Transmission is by autoinoculation from genital secretions although eye-to-eye spread may occur. The incubation period is about 1 week.

Clinical features

1. **Presentation** is with a subacute onset of unilateral or bilateral mucopurulent discharge. Unlike adenoviral infection, the conjunctivitis becomes chronic and may persist for 3–12 months if untreated.
2. **Signs**
   - Scant mucopurulent discharge.
   - Large follicles, most prominent in the interior fornical conjunctiva (Fig. 4.24), which may also involve the upper tarsal conjunctiva (Fig. 4.25).
   - Peripheral corneal infiltrates may appear 2–3 weeks after the onset of conjunctivitis (Fig. 4.26).
   - Tender lymphadenopathy.

Fig. 4.24
Large conjunctival follicles in adult chlamydial infection

Fig. 4.25
Conjunctival follicles in adult chlamydial infection

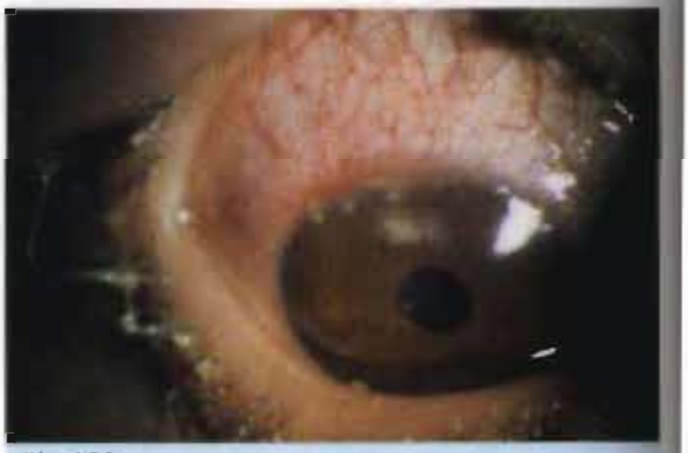

Fig. 4.26
Marginal infiltrates in adult chlamydial infection

Fig. 4.27
Superior micropannus in long-standing adult chlamydial infection

- Long-standing cases are characterized by less prominent follicles and the development of mild conjunctival scarring and a superior pannus (Fig. 4.27).

Laboratory investigations

Confirmation of clinical diagnosis can be achieved through laboratory tests. In view of the venereal nature of the disease, referral to a genitourinary clinic is mandatory for investigation and management of other possible sexually transmitted diseases. Currently used tests include:

1. **Direct monoclonal fluorescent antibody microscopy** of conjunctival smears, which is rapid and inexpensive.
2. **Enzyme-linked Immunosorbent assay** for chlamydial antigens.
3. **Standard single-passage McCoy cell culture**, which requires at least 3 days.
4. **Polymerase chain reaction.**

Treatment

1. **Topical** treatment is with tetracycline ointment q.i.d. for 6 weeks.
2. **Systemic** therapy is with one of the following:
   - Azithromycin 1 g as a single dose.
   - Doxycycline 100 mg b.d. for 1–2 weeks.
   - Erythromycin 500 mg q.i.d. for 1 week if tetracycline is inappropriate.

NB: It is essential that sexual partners are identified and treated.

Neonatal chlamydial conjunctivitis

Chlamydial infection is the most common cause of neonatal conjunctivitis and is notifiable. It may be associated with systemic chlamydial infection which may result in otitis, rhinitis and pneumonitis. Because the infection is transmitted from the mother during delivery it is important that both parents are examined for evidence of genital infection.

Fig. 4.28
Mucopurulent discharge in neonatal chlamydial infection

1. **Presentation** is usually 5–19 days after birth.
2. **Signs.** Mucopurulent discharge (Fig. 4.28) and a papillary conjunctival reaction because infants cannot form follicles until about the third month of life. Occasional complications, if untreated, include conjunctival scarring and superior corneal pannus.
3. **Treatment** is with topical tetracycline and oral erythromycin ethyl succinate 25 mg/kg body weight b.d. for 2 weeks.

NB: Systemic tetracycline is contraindicated in children under the age of 12 as well as pregnant or breast-feeding women because it may cause dental staining and occasionally hypoplasia in offspring.

Trachoma

Trachoma is an infection caused by serotypes A, B, Ba and C of *Chlamydia trachomatis*. It is a disease of underprivileged populations with poor conditions of hygiene. The common fly is the major vector in the infection–reinfection cycle. Currently trachoma is the leading cause of preventable blindness in the world.

Fig. 4.29
Conjunctival follicles and papillae in early active trachoma

Clinical features and treatment

1. **Presentation** is during childhood with a mixed follicular/papillary conjunctivitis (Fig. 4.29). In children under the age of 2 years the papillary component may predominate.

Fig. 4.30
Mild conjunctival scarring in chronic trachoma

2. **Chronic conjunctival inflammation** results in fine linear or stellate scars in milder cases (Fig. 4.30), or broad confluent scars (Arlt lines) (Fig. 4.31) in severe cases. The entire conjunctiva is involved but the effects are most prominent on the upper tarsus.
3. **Limbal follicles** are a unique feature. They later cicatrize and become covered by epithelium, resulting in an uneven surface (Herbert pits) (Fig. 4.32).
4. **Keratitis**, during the inflammatory stage, ranges from superior epithelial keratitis to anterior stromal infiltrates and pannus formation (Fig. 4.33).
5. **Progressive conjunctival scarring**, if severe, causes distortion of the eyelids, particularly of the upper tarsus (Fig. 4.34), to produce trichiasis (Fig. 4.35) and cicatricial entropion (Fig. 4.36). It may also destroy conjunctival goblet cells and involve the ductules of the lacrimal gland, resulting in a dry eye.
6. **End-stage trachoma** is characterized by severe corneal ulceration and opacification.
7. **Treatment** is with a single dose of azithromycin 1 g. The most important preventive measure is strict personal hygiene.

Fig. 4.31
Conjunctival scarring (Arlt line) in chronic trachoma

Fig. 4.33
Trachomatous pannus

Fig. 4.32
Herbert pits in trachoma

Fig. 4.34
Severe conjunctival scarring in trachoma

Fig. 4.35
Trichiasis and corneal vascularization in advanced trachoma

Fig. 4.36
Entropion of the upper eyelid in advanced trachoma (Courtesy of C. Barry)

World Health Organization grading of trachoma

TF = trachoma follicles with five or more on the superior tarsus.
TI = trachomatous inflammation diffusely involving the tarsal conjunctiva, which obscures 50% or more of the normal deep tarsal vessels.
TS = trachomatous conjunctival scarring.
TT = trachomatous trichiasis touching the cornea.
CO = corneal opacity.

Allergic inflammations

Allergic rhinoconjunctivitis

Allergic rhinoconjunctivitis, the most common form of ocular and nasal allergy, is a hypersensitivity reaction to specific airborne antigens.

Fig. 4.37
Allergic rhinoconjunctivitis

1. **Classification**
   a. Seasonal allergic rhinoconjunctivitis, with onset of 'hay fever' during the summer, is the commonest and mildest form of allergic conjunctivitis. The most common allergens are pollens.
   b. Perennial allergic rhinoconjunctivitis causes symptoms throughout the year with exacerbation in the autumn when exposure to dust mites and fungal allergens is greatest. It is less prevalent and milder than the seasonal type but more persistent.
2. **Presentation** is with transient, acute attacks of redness, watering and itching, associated with sneezing and nasal discharge.
3. **Signs**
   - Lid oedema.
   - The conjunctiva has a milky (Fig. 4.37) or pinkish appearance as a result of oedema and injection.
   - Small papillae may occur on the upper tarsal conjunctiva.
4. **Treatment** is with either a topical mast cell stabilizer (nedocromil, lodoxamide) or a topical antihistamine (levocabastine, azelastine or emedastine) b.d. to q.i.d. when the patient is symptomatic. Otopatadine 0.1% is both an antihistamine and a mast cell stabilizer which is effective when used b.d. Lotepredol etabonate 0.5% q.i.d. may also be helpful.

Vernal keratoconjunctivitis

Vernal keratoconjunctivitis (VKC) is a recurrent, bilateral, external, ocular inflammation primarily affecting boys and young adults living in warm, dry climates. It is an allergic disorder in which IgE and cell-mediated immune mechanisms play an important role. About three-quarters of patients have associated atopy and two-thirds have a family history of atopy. Such patients often develop asthma and eczema in infancy. The onset of VKC is usually after the age of 5 years and the condition eventually resolves around puberty, only rarely persisting beyond the age of 25 years. VKC may

occur on a seasonal basis, with a peak incidence over late spring and summer, although many patients have year-round disease. Patients with VKC have a higher incidence of keratoconus as well as other types of corneal ectasia such as pellucid marginal degeneration and keratoglobus.

The main symptoms are intense ocular itching which may be associated with lacrimation, photophobia, foreign body sensation and burning. Thick mucus discharge and ptosis also occur. The three main clinical types are: (a) *palpebral*, (b) *limbal* and (c) *mixed*. Limbal signs are more common in dark-skinned races, while tarsal and corneal signs predominate in lighter-skinned races. It is, however, likely that many mild or atypical forms may be unrecognized because no precise diagnostic criteria have been established. The long-term prognosis is good.

Clinical features

1. **Palpebral VKC** (in chronological order)
   - Diffuse papillary hypertrophy, most marked on the superior tarsus (Fig. 4.38).
   - The papillae enlarge and have a flat-topped polygonal appearance reminiscent of cobblestones (Fig. 4.39).
   - In severe cases, the connective tissue septa rupture, giving rise to giant papillae, which may be coated by copious mucus (Fig. 4.40).
   - As the inflammation settles the papillae shrink and become more separated but often do not disappear.
2. **Limbal VKC** is characterized by mucoid nodules scattered around the limbus with discrete white superficial spots (Trantas dots) composed predominantly of eosinophils at the apices of the lesions (Fig. 4.41).

Keratopathy

This is common and may take the following forms:

1. **Punctate epithelial erosions** involving the superior cornea are the earliest findings.
2. **Shield ulceration** (Fig. 4.42) is a serious problem which may be complicated by bacterial keratitis and rarely perforation.

Fig. 4.38
Conjunctival hyperaemia and diffuse papillary hypertrophy in mild vernal disease

Fig. 4.40
Giant papillae and copious mucus in advanced vernal disease (Courtesy of A. Bacon)

Fig. 4.39
'Cobblestone' papillae in severe vernal disease

Fig. 4.41
Limbal nodules with overlying fine white plaques (Trantas dots) in vernal limbitis

3. **Plaque formation** (Fig. 4.43) may occur when the base of the ulcer becomes coated with desiccated mucus. This results in defective wetting by tears, prevents re-epithelialization and predisposes to subepithelial scarring and vascularization.
4. **Pseudogerontoxon** resembles an arcus senilis and is usually characterized by a 'cupid's bow' outline in a previously inflamed segment of the limbus (Fig. 4.44).

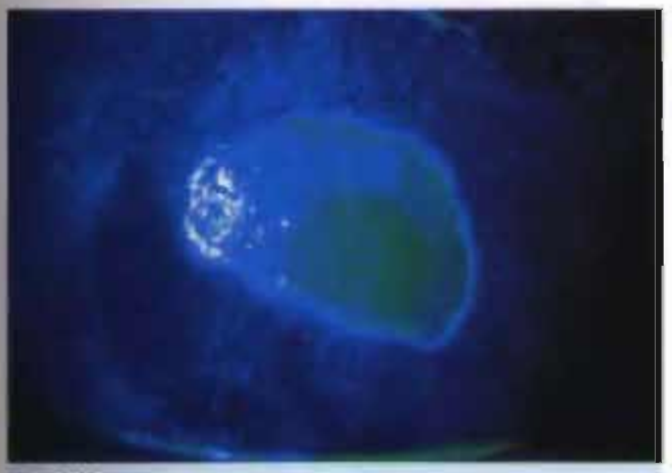

Fig. 4.42
Shield-like corneal ulceration stained with fluorescein in vernal disease (Courtesy of C. Barry)

Fig. 4.43
Corneal plaque in vernal disease

Fig. 4.44
Pseudogerontoxon in vernal disease

Treatment

1. **Topical**
   - *a.* ***Steroids*** are indicated mainly for keratopathy although they may be required as short-term therapy for severe discomfort in patients with only conjunctival involvement. Fluorometholone should be used since it has a weaker ocular hypertensive effect than dexamethasone and prednisolone. It is often possible to discontinue steroids between attacks and treat exacerbations vigorously with high doses, tapering to a relatively small dose as quickly as possible.
   - *b.* ***Mast cell stabilizers*** such as nedocromil b.d. and lodoxamide q.i.d. are used as prophylactic therapy that reduces the need for steroids. They do not have the side effects of steroids and can therefore be used for prolonged periods but are not effective in controlling acute exacerbations.
   - *c.* ***Antihistamines*** such as levocabastine are also effective.
   - *d.* ***Acetylcysteine 0.5%*** has mucolytic properties and is useful in the treatment of early plaque formation.
   - *e.* ***Cyclosporin 2%*** may be useful in steroid-resistant cases but is not yet widely available.
2. **Supratarsal steroid injection** of betamethasone or triamcinolone is effective in patients with severe disease unresponsive to conventional therapy.
3. **Surgical** treatment may be required for severe shield ulcers resistant to medical therapy. This may involve debridement, superficial keratectomy, excimer laser phototherapeutic keratectomy as well as amniotic membrane transplantation to enhance re-epithelialization.

Atopic keratoconjunctivitis

Atopic keratoconjunctivitis (AKC) is a relatively rare, but potentially serious, condition which typically affects young men with atopic dermatitis (*see* Chapter 20). Patients with atopic dermatitis may develop ocular involvement several years after the onset of other atopic features. Ocular manifestations are similar to, but not the same as, those associated with VKC, although occasionally AKC may be a direct sequel of childhood VKC. Unlike VKC, which usually resolves spontaneously, AKC persists for many years and is associated with a high rate of significant visual morbidity. Patients with atopic dermatitis may also develop visual impairment from keratoconus, presenile cataract and rarely retinal detachment.

Clinical features

1. **The lids** are red, thickened, macerated and fissured (*see* Fig. 1.19). Associated chronic staphylococcal blepharitis is very common.

2. **Conjunctivitis** primarily involves the inferior forniceal and tarsal conjunctiva.
   - Infiltration of the tarsal conjunctiva results in an overall pale and featureless appearance (Fig. 4.45).
   - During exacerbations there may be chemosis, limbal hyperaemia and papillary hypertrophy (Fig. 4.46).
   - In advanced cases cicatrizing conjunctivitis may develop with inferior forniceal shortening and symblepharon formation (Fig. 4.47).
3. **Keratopathy** is the main cause of visual impairment and is characterized by the following:
   - Punctate epithelial erosions are common (Fig. 4.48).
   - More advanced lesions include persistent epithelial defects, shield-shaped anterior stromal scars (Fig. 4.49) and peripheral vascularization.
4. **Complications** include aggressive herpes simplex keratitis and microbial keratitis.

Fig. 4.45
Tarsal conjunctival infiltration in atopic disease

Treatment

This is similar to that of VKC but is more difficult and prolonged.

1. **Topical**
   a. Antibiotics and lid hygiene for associated staphylococcal blepharitis (*see* Chapter 1).

Fig. 4.46
Mild conjunctival papillary hypertrophy in atopic disease

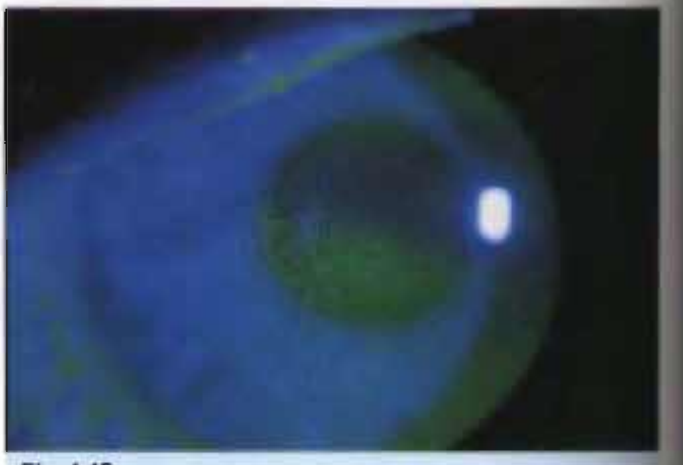

Fig. 4.48
Extensive punctate epithelial erosions in atopic disease

Fig. 4.47
Conjunctival scarring in advanced atopic disease

Fig. 4.49
Shield-like anterior stromal scarring in atopic disease

b. ***Preservative-free lubricants*** may be useful during exacerbations.
c. ***Steroids*** are effective as short-term treatment of severe inflammatory exacerbations and for keratopathy.
d. ***Mast cell stabilizers*** such as sodium cromoglycate, nedocromil and lodoxamide are effective and should be used throughout the year as prophylaxis against exacerbation and as steroid-sparing agents.
e. ***Non-steroidal anti-inflammatory agents*** such as ketolorac are also effective and may be used in combination with a mast cell stabilizer.
f. ***Antihistamines*** are less effective in AKC than in VKC.
g. ***Cyclosporin 2%*** is effective and safe.

2. **Supratarsal steroid injections** should be considered when topical treatment is ineffective.
3. **Systemic**
   a. ***Antihistamines*** may be useful for severe itching.
   b. ***Antibiotics*** such as azithromycin 500 mg once daily for 3 days may be effective in reducing inflammation aggravated by staphylococci.
   c. ***Cyclosporin*** in severe cases.

Blistering mucocutaneous diseases

Cicatricial pemphigoid

Cicatricial pemphigoid is an idiopathic, subepidermal/subepithelial blistering and scarring autoimmune (type 2 hypersensitivity) disease characterized by autoantibodies that bind to basement membrane. The condition usually presents in late middle age and affects women more commonly than men (*see* Chapter 20). Conjunctival involvement (ocular cicatricial pemphigoid) commonly occurs in association with mucocutaneous lesions but occasionally may occur in isolation (pure ocular cicatricial pemphigoid). Ocular involvement is always bilateral, but frequently asymmetrical with regard to time of onset, severity and rate of progression.

Clinical features

1. **Presentation** is with an insidious onset of non-specific symptoms such as irritation, burning and tearing, so that the correct diagnosis may be easily overlooked.
2. **Signs** (in chronological order)
   - Papillary conjunctivitis associated with diffuse conjunctival hyperaemia.
   - Subconjunctival bullae may form and, on bursting, give rise to ulceration and the formation of pseudomembranes.
   - Subepithelial fibrosis, conjunctival shrinkage and flattening of the contour of the plica and caruncle (Fig. 4.50).

Fig. 4.50
Subconjunctival fibrosis and flattening of the plica in ocular cicatricial pemphigoid

Fig. 4.51
Active ocular cicatricial pemphigoid

   - The usually progressive course of the disease may be interrupted by episodes of subacute activity, characterized by diffuse conjunctival hyperaemia and oedema (Fig. 4.51).

Complications

1. **Dry eye** is caused by a combination of destruction of goblet cells and accessory lacrimal glands as well as occlusion of the main lacrimal ductules and meibomian gland orifices.
2. **Symblepharon** is a serious complication in which adhesions form between palpebral and bulbar conjunctiva. It is best seen early in the disease process by drawing the lower eyelid down and asking the patient to look up (Fig. 4.52).
3. **Ankyloblepharon** is characterized by the formation of adhesions at the outer canthi between the upper and lower eyelids (Fig. 4.53).
4. **Secondary keratopathy**, which may be sight-threatening, is caused by a combination of entropion due

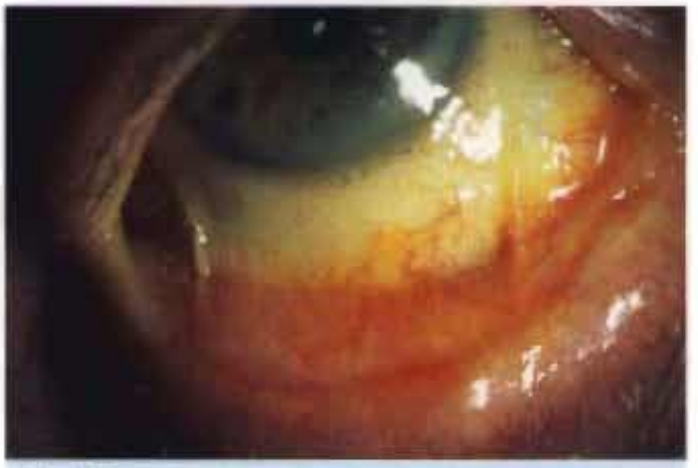

Fig. 4.52
Symblepharon in ocular cicatricial pemphigoid

Fig. 4.55
Total obliteration of the fornices in ocular cicatricial pemphigoid

Fig. 4.53
Ankyloblepharon in ocular cicatricial pemphigoid

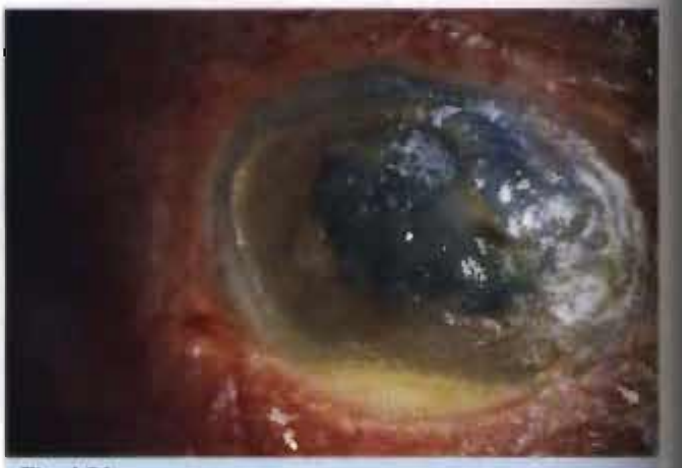

Fig. 4.56
Secondary bacterial keratitis in ocular cicatricial pemphigoid

Fig. 4.54
Total corneal keratinization in ocular cicatricial pemphigoid

to cicatrization of palpebral conjunctiva, metaplastic lashes (*see* Fig. 1.11), lagophthalmos secondary to symblepharon, dryness and limbal stem cell depletion.

5. **End-stage disease** is characterized by keratinization of the corneal surface (Fig. 4.54), obliteration of the fornices (Fig. 4.55), corneal vascularization and ulceration which may result in secondary bacterial infection (Fig. 4.56).

Treatment

1. **Topical**
   a. *Steroids* may be beneficial during the acute stage.
   b. *Tear substitutes* may be required to alleviate tear deficiency.
   c. *Antibiotics* should be used after cultures of the conjunctiva and lids have been taken.
2. **Subconjunctival mitomycin C** injection may be effective in preventing progressive conjunctival cicatrization.
3. **Silicone contact lenses** may be used with caution to protect the cornea from aberrant lashes and drying. Rigid scleral contact lenses may be effective in holding a tear film in front of the cornea and protecting it from lid friction and exposure, but do not prevent forniceal cicatrization.
4. **Systemic** treatment is required in the majority of cases.

a. ***Steroids*** are useful for the acute manifestations.
b. ***Dapsone*** may be useful for mild to moderate involvement.
c. ***Cytotoxic agents*** (methotrexate, cyclophosphamide) may be useful in suppressing conjunctival inflammatory activity and preventing progressive conjunctival shrinkage. Azathioprine is less effective when used alone but it may be of value when added to a partially effective agent.
d. ***Intravenous immunoglobulin*** therapy may be effective for resistant cases.

5. **Surgery** may be required for the following complications:
   - Cicatricial entropion and metaplastic lashes.
   - Severe dry eyes may require punctal occlusion if the puncta have not already been occluded by scarring.
   - Large, recurrent, corneal defects may require tarsorrhaphy or injection of botulinum toxin into the levator to induce ptosis to promote healing.
   - Keratoprostheses (*see* Chapter 5) may be beneficial in eyes with advanced keratinization of the ocular surface.

Stevens–Johnson syndrome

Stevens–Johnson syndrome is an acute, severe, mucocutaneous blistering disease, which primarily occurs in young healthy individuals. Males are affected more often than females. The exact aetiology is unknown, but an abnormal immunological reaction is the probable cause. The most common precipitating factor is hypersensitivity to drugs or viral infections. The basic lesion is an acute vasculitis which affects skin and mucous membranes in all patients and the conjunctiva in 90%. The disease is self-limiting, so that when the acute phase is controlled most patients recover with good function of affected tissues (*see* Chapter 20).

Clinical features

1. **Presentation** is with fever, malaise, sore throat, and possibly cough and arthralgia which may last up to 14 days.
2. **Signs**
   - Crusty eyelids associated with a transient, self-limiting papillary conjunctivitis is the most common feature (Fig. 4.57).
   - Severe membranous or pseudomembranous conjunctivitis with patchy conjunctival infarction and the development of focal fibrotic areas is less common (Fig. 4.58).

NB: Following the acute phase of the disease, no further scarring occurs.

Complications

1. **Symblepharon** formation and keratinization.
2. **Epiphora** caused by punctal obstruction.

Fig. 4.57
Acute conjunctivitis in Stevens–Johnson syndrome

Fig. 4.58
Residual focal conjunctival fibrosis in Stevens–Johnson syndrome

3. **Dry eye** resulting from obstruction of lacrimal gland ductules.
4. **Keratopathy** secondary to cicatricial entropion, aberrant lashes and conjunctival keratinization.

Treatment

1. **Systemic** steroids are usually necessary. Aciclovir is indicated if herpes simplex is suspected as causative.
2. **Topical steroids** administered early during the course of the disease may control vasculitis and prevent conjunctival infarction.
3. **A scleral ring**, consisting of a large haptic lens with the central zone removed, may be successful in preventing symblepharon formation during the acute stage of the disease.
4. **Other measures** include the use of topical retinoic acid for keratinization, tear supplements, therapeutic contact lenses, punctal occlusion and surgery to correct permanent deformities.

Miscellaneous inflammations

Superior limbic keratoconjunctivitis

Superior limbic keratoconjunctivitis (SLK) of Theodore is an uncommon, chronic inflammatory disorder which typically affects middle-aged women who may have associated thyroid dysfunction. SLK is frequently misdiagnosed because symptoms are more severe than signs. The condition is usually bilateral, although involvement may be asymmetrical. The course is prolonged, with remissions and exacerbations until eventual resolution occurs without sequelae.

Clinical features

1. **Presentation** is with non-specific symptoms such as foreign body sensation, burning, photophobia and mucoid discharge.

Fig. 4.59
Papillary hypertrophy in superior limbic keratoconjunctivitis

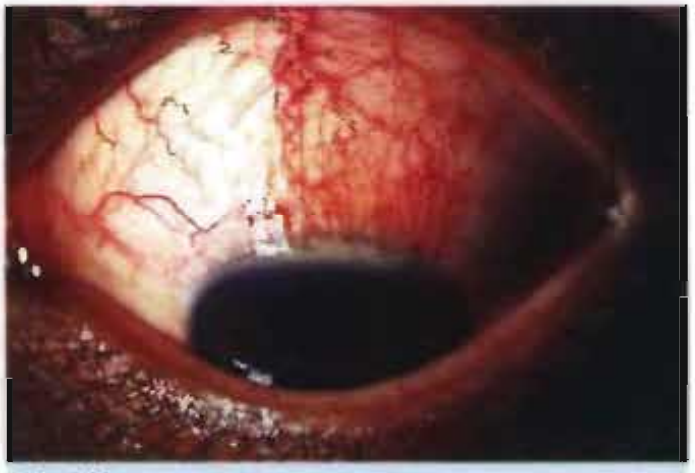

Fig. 4.60
Bulbar conjunctival hyperaemia and limbal papillary hypertrophy in superior limbic keratoconjunctivitis

2. **Signs**
   - Papillary hypertrophy of the superior tarsus which may give rise to a diffuse velvety appearance (Fig. 4.59).
   - Hyperaemia of the superior bulbar conjunctiva, which is most intense at the limbus and fades towards the superior fornix, and superior limbic papillary hypertrophy (Fig. 4.60). The conjunctival epithelial cells may become keratinized and the affected area may lack lustre.
   - Superior punctate epithelial erosions are common.
   - Superior filamentary keratitis occurs in about one-third of cases and is not necessarily associated with aqueous tear deficiency.
   - Keratoconjunctivitis sicca is present in about 25% of cases.

Treatment

This is aimed primarily at altering the abnormal mechanical interaction between the upper lid and the superior limbus. Although there is no definitive treatment, the following options are available:

1. **Tear substitutes** for associated dryness.
2. **Acetylcysteine** 5% may be helpful for filamentary keratitis.
3. **Occlusion of the upper puncta** is simple and usually effective.
4. **Soft contact lenses**, which intervene between the lid and the limbus, may be useful.
5. **Thermocauterization** of the superior bulbar conjunctiva is safe and often effective.
6. **Resection** of the superior limbal conjunctiva may help in resistant disease.

Parinaud oculoglandular syndrome

Parinaud oculoglandular syndrome is a rare condition which is most frequently caused by: (a) *cat-scratch disease* (see Chapter 20) and (b) *tularaemia*. Other causes include sporotrichosis, tuberculosis, syphilis, lymphogranuloma venereum and infectious mononucleosis as well as certain fungal, viral and rickettsial infections.

1. **Presentation** is with unilateral conjunctivitis and constitutional upset.
2. **Signs**. Unilateral granulomatous conjunctivitis with nodular elevations surrounded by follicles (Fig. 4.61), associated with severe and painful ipsilateral lymphadenopathy.
3. **Treatment** varies according to the cause. Cat-scratch disease responds to oral ciprofloxacin and co-trimoxazole.

Ligneous conjunctivitis

Ligneous conjunctivitis is a very rare disorder characterized by recurrent pseudomembranous lesions which may also

Fig. 4.61
Conjunctival granulomas and follicles in Parinaud oculoglandular syndrome

Fig. 4.62
Ligneous conjunctivitis (Courtesy of C. Barry)

involve the mouth, nasopharynx, trachea and vagina. Occasionally membrane formation may be triggered by minor trauma.

1. **Presentation** is in childhood with gradual onset of bilateral conjunctivitis which becomes chronic.
2. **Signs.** Wood-like pseudomembranous lesions of the tarsal conjunctiva (Fig. 4.62).
3. **Treatment** with topical cyclosporin is most effective. Other treatment modalities that have been tried with limited success include topical hyaluronidase, antibiotics, steroids, sodium cromoglycate and silver nitrate. Cryotherapy and surgical resection usually result in rapid recurrence.

Mucus fishing syndrome

The most frequent underlying disease which initiates the cycle of mucus fishing is keratoconjunctivitis sicca, although any condition that causes excess mucus production may be responsible. While trying to remove the excess mucus from the conjunctival sac, the patient traumatizes the conjunctival epithelium. This further increases mucus secretion, creating a vicious cycle. Mucus fishing should be suspected when appropriate treatment of an external ocular disease does not produce the expected result. On direct questioning, the patient may deny mucus fishing.

1. **Presentation** is usually in adult life with chronic mucoid discharge.
2. **Signs.** Isolated, well-circumscribed areas which stain heavily with rose bengal. Staining is usually maximal over the caruncle, plica, nasal and inferior bulbar conjunctivae, and inferior tarsal conjunctiva.
3. **Treatment** is of the underlying disorder responsible for excess mucus production. The patient should also be instructed not to touch or to attempt directly to remove mucus from the eye.

Toxic conjunctivitis

Over-the-counter non-prescription eye decongestants may be used as self medication for ocular redness and discomfort. Commonly used preparations may contain vascoconstrictors (e.g. naphazoline and phenylephrine) with or without antihistamines. If used inappropriately they may give rise to conjunctivitis with irritation, burning, foreign body sensation and redness. The diagnosis is made by exclusion after other causes of conjunctivitis have been considered. The patient who does not recognize cause and effect may not volunteer the information.

1. **Signs**
   a. ***Diffuse conjunctival hyperaemia***, the most frequent, is probably a rebound phenomenon following discontinuation of a vasoconstrictor, similar to that occurring with nasal preparations. The hyperaemia is associated with papillae on the upper (Fig. 4.63) and lower tarsal conjunctiva.
   b. ***Follicular conjunctivitis***, probably due to a toxic effect, is less common and is most prominent on the inferior forniceal conjunctiva (Fig. 4.64).
   c. ***Blepharoconjunctivitis***, due to hypersensitivity, is the least common and is characterized by oedema and hyperaemia of the lids and conjunctiva.

Fig. 4.63
Toxic papillary conjunctivitis

Fig. 4.64
Toxic follicular conjunctivitis

2. **Treatment** involves discontinuation of topical medication. It must be explained that symptoms may temporarily worsen and then improve. Follicular conjunctivitis may take many weeks to resolve, particularly if the drops have been used for a long time. In such cases topical steroids may shorten recovery time. Blepharoconjunctivitis may also respond to a short course of topical steroids.

Degenerations

Pinguecula

Pinguecula is an extremely common, innocuous, usually bilateral and asymptomatic condition.

1. **Signs.** Yellow-white deposits on the bulbar conjunctiva adjacent to the nasal or temporal limbus (Fig. 4.65).
2. **Treatment** is usually unnecessary because growth is very slow or absent. Occasionally, however, a pinguecula may become acutely inflamed (pingueculitis) and require a short course of a weak steroid such as fluorometholone.

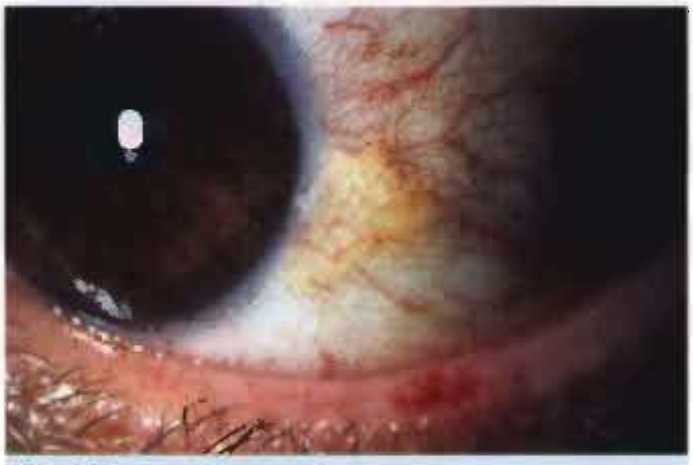

Fig. 4.65
Pinguecula

Pterygium

A pterygium is a triangular fibrovascular subepithelial ingrowth of degenerative bulbar conjunctival tissue over the limbus onto the cornea. Pterygia typically develop in patients who have been living in hot climates and may represent a response to chronic dryness and ultraviolet exposure.

Clinical features

1. **Signs** (in chronological order)
   - A small, grey, corneal opacity develops near the nasal limbus (Fig. 4.66).
   - The conjunctiva overgrows the opacity and progressively encroaches onto the cornea in a triangular fashion (Figs 4.67, 4.68).
   - A deposit of iron (Stocker line) may be seen in the corneal epithelium anterior to the advancing head of the pterygium.

Fig. 4.66
Early pterygium

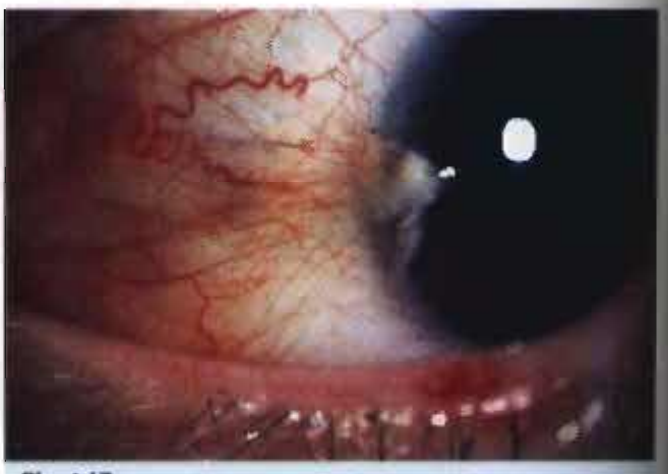

Fig. 4.67
Established pterygium

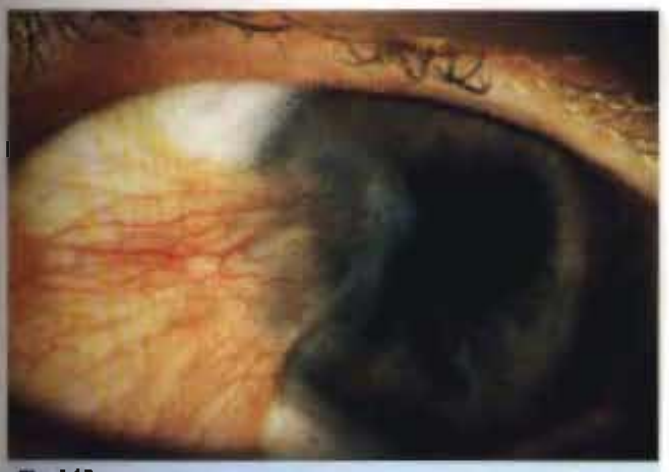

Fig. 4.68
Advanced pterygium

Fig. 4.69
Pterygium involving the visual axis

2. **Complications** include chronic irritation, decreased vision due to involvement of the visual axis (Fig. 4.69) or induced astigmatism, and disruption of the precorneal tear film. A pterygium may become intermittently inflamed and require a short course of a weak topical steroid.

Treatment

This is indicated either for cosmetic reasons or occasionally progression towards the visual axis. Simple excision is associated with a high rate of recurrence, frequently more aggressive than the initial lesion. Numerous techniques aimed at preventing recurrence have been described. Currently the most widely used technique involves excision of the pterygium and covering of the defect with either a conjunctival autograft or amniotic membrane. Adjunctive treatment with mitomycin C and beta-irradiation may be used to minimize recurrence but may rarely be complicated by late scleral necrosis.

Fig. 4.70
Pseudopterygium

Differential diagnosis

1. **A pseudopterygium** is caused by the adhesion of a fold of conjunctiva to a peripheral corneal ulcer or area of peripheral thinning, and is fixed only at its apex to the cornea (Fig. 4.70). A true pterygium is adherent to underlying structures throughout.
2. **Conjunctival intraepithelial neoplasia** (*see* below).

Concretions

Concretions are extremly common lesions which most frequently affect elderly patients and may also occur in chronic meibomian gland disease.

1. **Signs.** Small, often multiple, chalky, yellow-white deposits most commonly seen in the inferior tarsal and forniceal conjunctiva (Fig. 4.71).
2. **Treatment** is usually unnecessary because concretions are subepithelial and asymptomatic. If a large concretion erodes through the epithelium and causes irritation

Fig. 4.71
Conjunctival concretions

Fig. 4.72
Conjunctival retention cyst

it can be removed under topical anaesthesia with a needle.

Retention cyst

A retention cyst is a very common, usually asymptomatic, thin-walled lesion containing clear fluid (Fig. 4.72). Treatment, if appropriate, is by simple puncture with a needle.

Pigmented lesions

Conjunctival epithelial melanosis

Conjunctival (racial) epithelial melanosis is a benign condition often seen in dark-skinned individuals. Both eyes are affected but the intensity may be asymmetrical.

1. **Presentation** is during the first few years of life. The melanosis becomes static by early adulthood.
2. **Signs**
   - Areas of flat, patchy, brownish pigmentation scattered throughout the conjunctiva (Fig. 4.73).
   - With the slit-lamp the pigmentation is seen to be within the epithelium and therefore moves freely over the surface of the globe.
   - The lesions may be more intense at the limbus and around the perforating branches of the anterior ciliary vessels as they enter the sclera.
   - Juxtalimbal pigmentation may extend onto the peripheral cornea.
3. **Differential diagnosis**
   a. ***Conjunctival freckle*** is a tiny area of epithelial pigmentation (Fig. 4.74).
   b. ***Axenfeld loop*** is an area of melanosis around an intrascleral nerve or an anterior ciliary artery (Fig. 4.75).
   c. ***Mascara deposits*** usually accumulate in the inferior fornix (Fig. 4.76).
   d. ***Adrenochrome*** deposits are tiny clumps of pigment on the tarsal or forniceal conjunctiva associated with the

Fig. 4.74
Conjunctival freckle

Fig. 4.73
Conjunctival epithelial melanosis

Fig. 4.75
Melanosis around an intrascleral nerve

Fig. 4.76
Forniceal mascara deposits

Fig. 4.78
Congenital subepithelial melanocytosis (Courtesy of B. Jay)

Fig. 4.77
Conjunctival adrenochrome deposits

Fig. 4.79
Right congenital dermal melanocytosis in naevus of Ota

long-term use of adrenaline drops for glaucoma (Fig. 4.77).

Congenital ocular melanocytosis

Classification

Congenital ocular melanocytosis is an uncommon melanocytic hyperplasia which occurs in three clinical settings:

1. **Ocular melanocytosis**, the least common, involves only the eye.
2. **Dermal melanocytosis** involves only the skin and accounts for about one-third of cases.
3. **Oculodermal melanocytosis** (naevus of Ota) involves both skin and eye. It is the most frequently encountered type.

Clinical features

1. Signs
   - Multifocal, slate-grey pigmentation which lies subconjunctivally in the episclera and cannot be moved over the globe (Fig. 4.78).
   - Occasionally the peripheral cornea may be involved.

2. Naevus of Ota
   - Unilateral deep hyperpigmentation of facial skin, most frequently in the distribution of the first and second divisions of the trigeminal nerve (Fig. 4.79). It may be subtle in fair-skinned individuals and is best detected by observation in good lighting.
   - Involvement of the third division of the trigeminal nerve and of the nasal and buccal mucosa is uncommon.

Fig. 4.80
Right congenital conjunctival subepithelial melanocytosis and right iris hyperchromia in naevus of Ota

Fig. 4.81
Iris mammillations in naevus of Ota

Fig. 4.82
Fundus hyperpigmentation in naevus of Ota

Ipsilateral associations

1. **Iris hyperchromia** is common (Fig. 4.80).
2. **Iris mammillations**, which are tiny, regularly spaced, villiform lesions, are uncommon (Fig. 4.81). They may also be found in patients with neurofibromatosis-1, Axenfeld–Rieger anomaly and Peters anomaly.
3. **Fundus hyperpigmentation** is uncommon (Fig. 4.82).
4. **Melanoma** of the uveal tract, orbit, optic nerve head or brain may develop in a minority of white people.
5. **Glaucoma**, associated with trabecular hyperpigmentation, develops in about 10% of cases.

Conjunctival naevus

A conjunctival naevus is a relatively uncommon, benign, usually unilateral condition. The most common location is the juxtalimbal area (Fig. 4.83), followed by the plica and caruncle (Fig. 4.84).

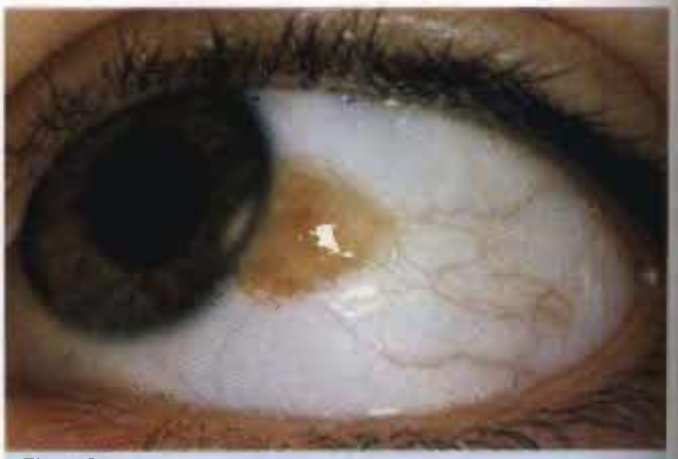

Fig. 4.83
Non-pigmented conjunctival naevus

1. **Presentation** is usually during the first two decades of life with ocular irritation or a pigmented lesion.
2. **Signs**
   - Solitary, sharply demarcated, flat or slightly elevated intraepithelial lesion which can be moved freely over the scleral surface. Cystic spaces within the naevus are frequent.
   - The extent of pigmentation is variable and some may be virtually non-pigmented (*see* Fig. 4.83).
   - Pigmented naevi virtually always contain some shade of brown, ranging from tan to deep chocolate (Fig. 4.85).
   - Around puberty the naevus may enlarge and become more pigmented.
3. **Signs of potential malignancy**
   - An unusual site such as palpebral or forniceal conjunctiva.
   - Extension onto the cornea.
   - Sudden increase in pigmentation or growth.
   - Development of vascularity except at puberty.
4. **Treatment** by excision is indicated mainly for cosmetic reasons. Less common indications include irritation and suspicion of malignant transformation.

Fig. 4.84
Caruncular naevus

Fig. 4.85
Pigmented conjunctival naevus

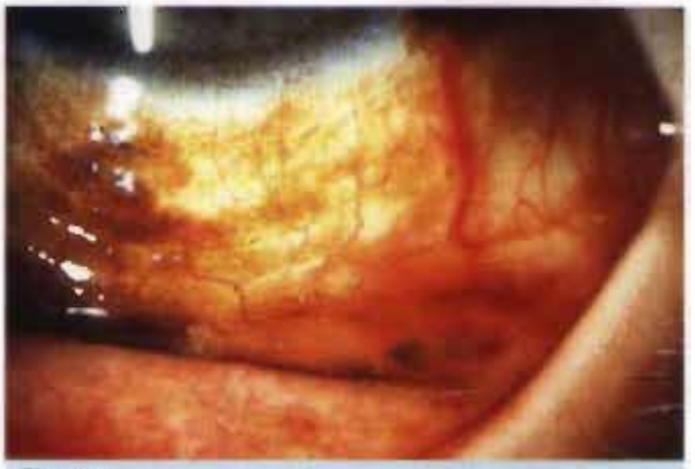

Fig. 4.87
Primary acquired melanosis

Primary acquired melanosis

Classification

Primary acquired melanosis (PAM) is an uncommon, almost always unilateral condition which typically affects middle-aged white people. The two histological types are as follows:

1. **PAM without atypia** is a benign proliferation of normal melanocytes, confined to the basal layer of the conjunctiva.
2. **PAM with atypia** is a pre-malignant condition with a 50% chance of malignant transformation within 5 years. It is characterized by an increase in number of large melanocytes with prominent nucleoli, involving all layers of the conjunctiva (pagetoid spread).

Fig. 4.88
Melanoma associated with primary acquired melanosis (Courtesy of B. Jay)

Clinical features

1. **Presentation** of PAM without atypia can be at any age, but PAM with atypia is usually seen after the age of 45 years.
2. **Signs**
   - Irregular, unifocal or multifocal areas of flat, brown pigmentation which may involve any part of the conjunctiva (Figs 4.86, 4.87).
   - The lesions involve the epithelium and can therefore be moved over the surface of the globe.

Fig. 4.86
Primary acquired melanosis (Courtesy of B. Jay)

- PAM may shrink or remain stable for long periods of time. It may also lighten, darken focally, or enlarge centrifugally (radial growth).

NB: Multiple biopsies assisted by immunohistochemistry are required for diagnosis because the clinical features of PAM with and without atypia are the same. A sign of malignant transformation of PAM to melanoma is the sudden appearance of one or more nodules in otherwise flat lesions (Fig. 4.88).

Treatment

1. **PAM without atypia** does not require treatment.
2. **PAM with atypia**
   - Small areas are treated by excision.
   - Larger areas that cannot be excised may be treated with cryotherapy or by topical application of mitomycin C.

Conjunctival melanoma

Conjunctival melanoma accounts for about 2% of all ocular malignancies.

Classsification

1. **Melanoma arising from PAM with atypia** accounts for 75% of cases (Fig. 4.89).
2. **Melanoma arising from a pre-exlsting naevus** accounts for 20%.
3. **Primary melanoma** is the least common.

Primary melanoma

1. **Presentation** is in the sixth decade except in patients with the rare dysplastic naevus syndrome, who develop multiple melanomas earlier.
2. **Slgns**
   - A solitary, black or grey nodule containing dilated feeder vessels which may become fixed to episclera (Fig. 4.90).

Fig. 4.89
Multifocal melanoma associated with primary acquired melanosis

Fig. 4.90
Primary pigmented conjunctival melanoma (Courtesy of B. Jay)

Fig. 4.91
Primary amelanotic conjunctival melanoma

   - Amelanotic tumours are pink and have a characteristic smooth, fish-flesh appearance (Fig. 4.91).
   - A common site is the limbus although the tumour may arise anywhere in the conjunctiva.

Treatment

1. **Circumscribed melanoma**
   - Surgical excision with a wide clearance and cryotherapy to prevent recurrence.
   - If histology reveals incomplete clearance, wide re-excision of the surgical scar and further cryotherapy are indicated.
   - Re-examination of the patient is at 6–12-monthly intervals for life. At each visit the entire conjunctival surface is examined and any suspicious areas examined histologically following biopsy or impression cytology.
2. **Diffuse melanoma** is treated by excision of localized nodules and cryotherapy or mitomycin C to the diffuse component (Fig. 4.92).
3. **Orbital recurrences** are treated by local resection and radiotherapy (Fig. 4.93). Exenteration does not improve

Fig. 4.92
Diffuse conjunctival melanoma

Fig. 4.93
Recurrence of conjunctival melanoma

the survival rate and is therefore reserved for patients with extensive and aggressive disease that cannot be controlled by other methods.

4. **Lymph node involvement** is treated by surgical excision and radiotherapy.
5. **Palliation** is with chemotherapy for metastatic disease.

Prognosis

The overall mortality is about 12% at 5 years and 25% at 10 years. The main sites for metastases are regional lymph nodes, lung, brain and liver. Poor prognostic indicators include:

- Multifocal tumours.
- Extralimbal tumours involving the caruncle, fornix or palpebral conjunctiva.
- Tumour thickness of 2 mm or more.
- Recurrence.
- Lymphatic or orbital spread.

Fig. 4.94
Large conjunctival naevus

Fig. 4.95
Conjunctival melanocytoma

Differential diagnosis

1. **A large naevus** that is growing during puberty (Fig. 4.94). However, unlike melanoma it does not involve the cornea.
2. **Ciliary body melanoma** with extraocular extension (*see* Fig. 11.22).
3. **Melanocytoma** is a rare, congenital, black, slow-growing lesion which cannot be moved freely over the globe (Fig. 4.95).
4. **Pigmented conjunctival carcinoma** in a dark-skinned individual.

Squamous tumours

Conjunctival papilloma

Pedunculated papilloma

This is caused by infection with human papillomavirus (types 6 and 11), which may occur by mother-to-infant transmission at birth through an infected vagina.

Fig. 4.96
Pedunculated conjunctival papillomas

1. **Presentation** may be early after birth or years later.
2. **Signs**. The papillomas, which may be multiple and occasionally bilateral, are most frequently located in the palpebral conjunctiva, fornix or caruncle (Fig. 4.96).

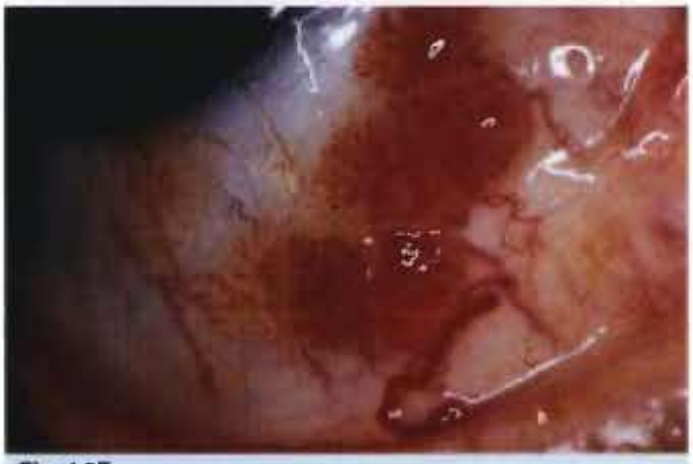

Fig. 4.97
Sessile conjunctival papilloma

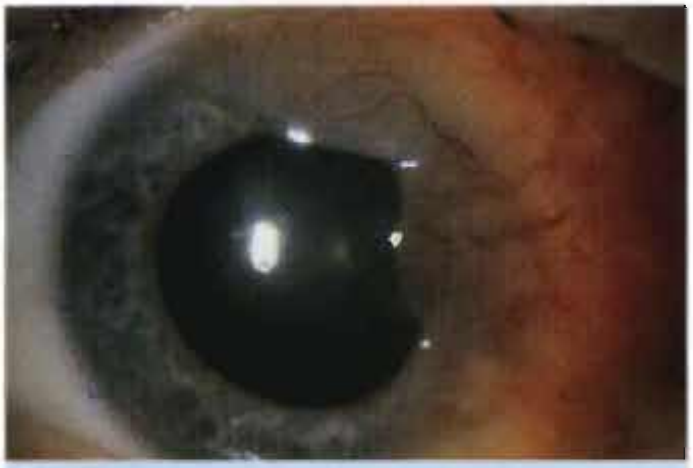

Fig. 4.98
En-plaque conjunctival intraepithelial neoplasia

Fig. 4.99
Papillomatous conjunctival intraepithelial neoplasia (Courtesy of C. Barry)

3. **Treatment** of small lesions may not be required because they often resolve spontaneously. Large lesions are treated by excision biopsy or cryotherapy. Treatment options for recurrences include subconjunctival interferon alpha, topical mitomycin C or oral cimetidine (Tagamet).

Sessile papilloma

Sessile (neoplastic) papilloma is not infectious.

1. **Presentation** is usually in middle age.
2. **Signs.** The lesion is single, unilateral and most frequently located on the bulbar and juxtalimbal conjunctiva (Fig. 4.97).
3. **Treatment** is by excision.

Conjunctival and corneal intraepithelial neoplasia

Conjunctival and corneal intraepithelial neoplasia (CCIN) is an uncommon, benign, slowly progressive unilateral disease with low malignant potential. Histological changes range from mild to severe epithelial dysplasia confined to the basal third of the epithelium to full-thickness epithelial involvement with dysplastic cells (carcinoma in situ). Risk factors include ultraviolet light exposure, human papilloma virus infection and AIDS.

Clinical features

1. **Presentation** is usually in late adult life with ocular irritation or a mass.
2. **En plaque** CCIN is a raised, gelatinous or leucoplakic growth with tufts of superficial blood vessels at the limbus within the interpalpebral fissure (Fig. 4.98).
3. **Papillomatous** CCIN is a raised discrete lesion with surface corkscrew-like blood vessels (Fig. 4.99).
4. **Diffuse** CCIN, which is uncommon, is characterized by indistinct conjunctival thickening (Fig. 4.100).

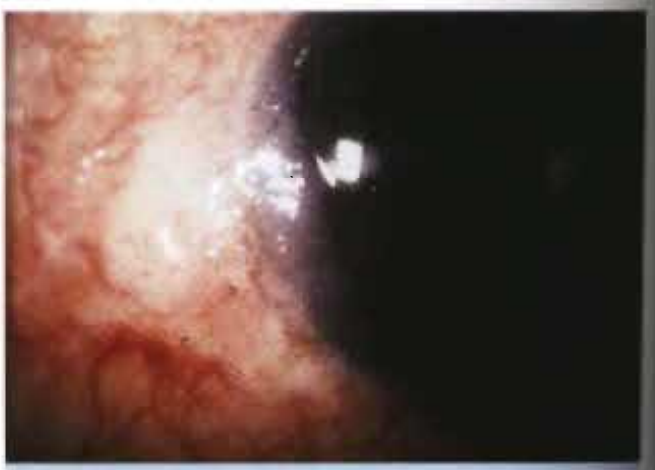

Fig. 4.100
Diffuse conjunctival intraepithelial neoplasia

NB: All three varieties may be associated with grey-white hyperplastic epithelium that extends onto the cornea. Impression cytology may be useful in diagnosis.

Treatment

1. **Localized** CCIN is treated by excision with adjunctive cryotherapy.
2. **Diffuse** CCIN is more difficult to treat because the poorly defined borders render involved tissue clinically indistinguishable from healthy tissue. This frequently results in incomplete excision and a high rate of recurrence. Other treatment modalities have therefore been introduced either as alternatives or adjuncts to surgery. These include topical mitomycin C, 5-fluorouracil and interferon alpha-2b.

Differential diagnosis

1. **Atypical conjunctival papilloma.**
2. **Pterygium**, which is also associated with exposure to ultraviolet radiation.
3. **Pseudo-epitheliomatous hyperplasia**, which is a rapidly growing, white, hyperkeratotic, juxtalimbal nodule which develops secondary to irritation (Fig. 4.101).
4. **Unilateral chronic conjunctivitis**, which may be mimicked by diffuse CCIN.
5. **Amelanotic melanoma.**
6. **Conjunctival carcinoma** (*see* below).

Conjunctival squamous cell carcinoma

Conjunctival squamous cell carcinoma is a rare, slow-growing tumour of low-grade malignancy which may arise *de novo* or from pre-existing CCIN. It occurs with increased frequency in patients with xeroderma pigmentosum and AIDS.

Fig. 4.101
Pseudo-epitheliomatous conjunctival hyperplasia

Clinical features

1. **Presentation** is usually in late adult life in a similar way to CCIN.
2. **Signs**
   - A fleshy, pink, papillomatous or gelatinous mass, often associated with feeder vessels (Fig. 4.102), which may sometimes be covered by plaques of keratin.
   - The tumour is most frequently juxtalimbal and seldom arises from forniceal or palpebral conjunctiva.
   - Limbal tumours may involve adjacent cornea (Fig. 4.103) but scleral (deep) invasion is uncommon.

Treatment

1. **Surgical excision** and adjunctive cryotherapy.
2. **Topical chemotherapy** with mitomycin C or 5-fluorouracil may be indicated for recurrences or primary treatment of selected early cases.
3. **Enucleation** in cases of intraocular invasion.
4. **Exenteration** for advanced cases with orbital involvement.

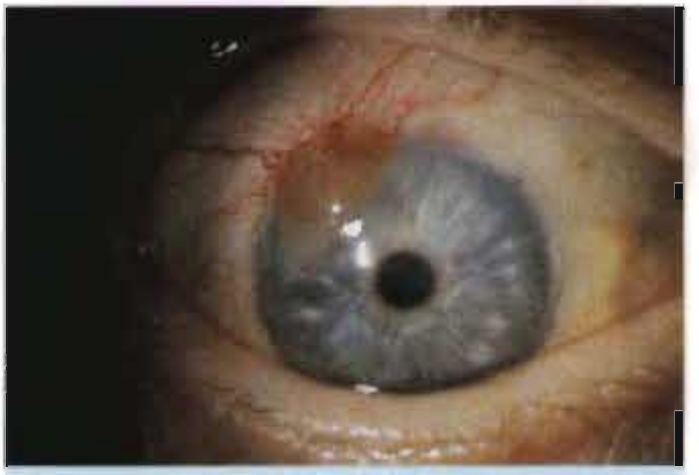

Fig. 4.102
Conjunctival squamous cell carcinoma invading the cornea

Fig. 4.103
Advanced conjunctival squamous cell carcinoma (Courtesy of C. Barry)

Miscellaneous tumours

Conjunctival sebaceous gland carcinoma

Sebaceous gland carcinoma is a very rare but aggressive tumour which may invade the orbit and metastasize to local lymph nodes as well as distant sites. It is seen in the following two clinical settings:

1. **Conjunctival intraepithelial invasion** of sebaceous gland carcinoma (pagetoid spread) from a tumour primarily involving the meibomian glands or glands of Zeis (*see* Chapter 1). In this setting it may mimic chronic blepharoconjunctivitis.
2. **Primary intraepithelial carcinoma** arising from and confined to the conjunctival epithelium is much less common (Fig. 4.104).

Epibulbar choristoma

A choristoma is a congenital overgrowth of normal tissue in an abnormal location. There are two main types: (a) *dermoids* and (b) *lipodermoids*.

Dermoid

Dermoids may occur in isolation or often in patients with Goldenhar syndrome (Fig. 4.105), Treacher Collins syndrome and naevus sebaceous syndrome of Jadassohn. Dermoids contain a variety of tissues such as cartilage, fat, muscle, hair follicles and sebaceous glands.

1. **Presentation** is in early childhood.
2. **Signs.** Smooth, soft, yellowish, subconjunctival masses most frequently located at the inferotemporal limbus (Fig. 4.106). Occasionally the lesions are very large and may virtually encircle the limbus (Fig. 4.107). Bilateral involvement is uncommon.
3. **Treatment** is indicated if the lesion causes a cosmetic deformity, extends to the visual axis, causes astigmatism

Fig. 4.104
Conjunctival intraepithelial sebaceous gland carcinoma

Fig. 4.106
Localized limbal dermoid

Fig. 4.105
Limbal dermoid in Goldenhar syndrome

Fig. 4.107
Large limbal dermoid

Fig. 4.108
Lipodermoid

or dellen formation, or chronic ocular irritation. Small lesions can be excised although the removal of large lesions may be more complicated and may require lamellar corneal or scleral grafting.

Lipodermoid

1. **Presentation** is in adult life.
2. **Signs.** Soft, movable, subconjunctival mass most commonly located at the outer canthus (Fig. 4.108).
3. **Treatment** should be avoided because surgery may be complicated by scarring, ptosis, dry eye and ocular motility problems. However, if they are particularly unsightly, then debulking the anterior portion may improve cosmesis without compromising ocular motility.

Conjunctival lymphoma

Lymphocytes normally reside in the substantia propria, so that the conjunctiva, similar to extranodal lymphoid sites such as the bowel and lung, may be the seat of lymphoproliferative lesions that constitute a spectrum ranging from benign reactive hyperplasia through atypical hyperplasia to lymphoma. Benign and malignant lesions share similar characteristics and cannot be differentiated clinically. Occasionally reactive hyperplasia undergoes malignant transformation to lymphoma. Most conjunctival lymphomas are of B-cell origin with systemic involvement in about 30% of cases.

1. **Presentation** is usually in late adult life with irritation or painless swelling.
2. **Signs.** Slow-growing, mobile, salmon-pink or flesh-coloured infiltrates in the inferior fornices or epibulbar surfaces which may be bilateral (Fig. 4.109). The lesions may be localized to the conjunctiva or associated with orbital involvement.

> *NB:* Rarely a diffuse lymphoma may mimic chronic conjunctivitis (Fig. 4.110).

3. **Treatment** is most frequently with radiotherapy. Other options include chemotherapy, excision, cryotherapy and local injection of interferon alpha-2b.

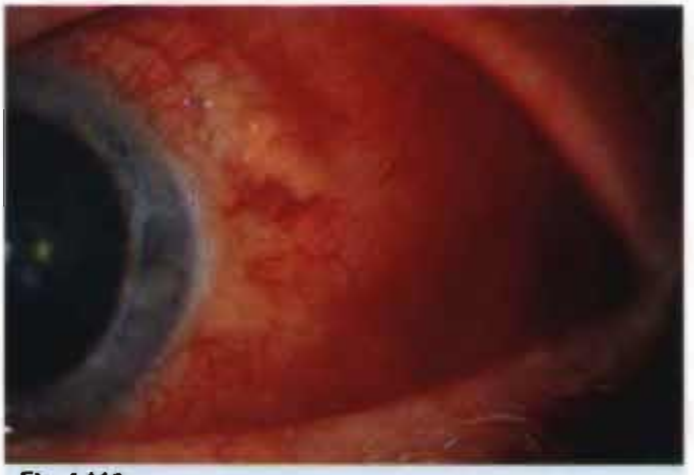

Fig. 4.110
Conjunctival lymphoma mimicking chronic conjunctivitis

Fig. 4.109
Conjunctival lymphoma

Fig. 4.111
Conjunctival Kaposi sarcoma

Conjunctival Kaposi sarcoma

Kaposi sarcoma is a slow-growing, low-grade malignancy which occurs in patients with AIDS.

Fig. 4.112
Conjunctival pyogenic granuloma

1. **Presentation** is in adult life with irritation or painless discoloration.
2. **Signs.** A flat, bright-red lesion, most often located in the inferior fornix which may be mistaken for a 'chronic' subconjunctival haemorrhage (Fig. 4.111).
3. **Treatment** is required for cosmetic reasons, bleeding or infection. Options include focal radiotherapy and excision with or without adjunctive cryotherapy.

Conjunctival pyogenic granuloma

A pyogenic granuloma is a vascularized proliferation of granulomatous tissue.

1. **Presentation** is frequently a few weeks after conjunctival surgery such as excision of a pterygium.
2. **Signs.** A fleshy, vascularized conjunctival mass (Fig. 4.112).
3. **Treatment** is by excision.

CHAPTER 5

Cornea

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Introduction

Applied anatomy

The average corneal diameter is 11.5 mm (vertical) and 12 mm (horizontal). The cornea consists of the following layers (Fig. 5.1):

1. **The epithelium** is stratified, squamous and non-keratinized, and comprises:
   - A single layer of basal columnar cells attached by hemidesmosomes to the underlying basement membrane.
   - Two to three rows of wing cells.
   - Two layers of squamous surface cells.
   - The surface area of the outermost cells is increased by microplicae and microvilli which facilitate the attachment of mucin. After a lifespan of a few days the superficial cells are shed into the tear film. Because of its excellent ability to regenerate, the epithelium does not scar.
   - The epithelial stem cells are principally located at the superior and inferior limbus and are indispensable for the maintenance of healthy corneal epithelium. They also act as a junctional barrier, preventing conjunctival tissue from growing onto the cornea. Dysfunction or deficiency of limbal stem cells may result in chronic epithelial defects, overgrowth of conjunctival epithelium onto the corneal surface and vascularization. Some of these problems may be prevented by limbal cell transplantation.
2. **Bowman layer** is the acellular superficial layer of the stroma which scars when damaged.
3. **The stroma** makes up 90% of corneal thickness. It is principally composed of regularly orientated layers of collagen fibrils whose spacing is maintained by proteoglycan ground substance (chondroitin sulphate and keratan sulphate) with interspersed modified fibroblasts (keratocytes).
4. **Descemet membrane** is composed of a fine latticework of collagen fibrils. It consists of an anterior banded zone which develops in utero and a posterior non-banded zone laid down throughout life by the endothelium.
5. **The endothelium** consists of a single layer of hexagonal cells. It plays a vital role in maintaining corneal deturgescence but cannot regenerate. With age, the number of cells gradually decreases and therefore neighbouring cells enlarge to fill the space.

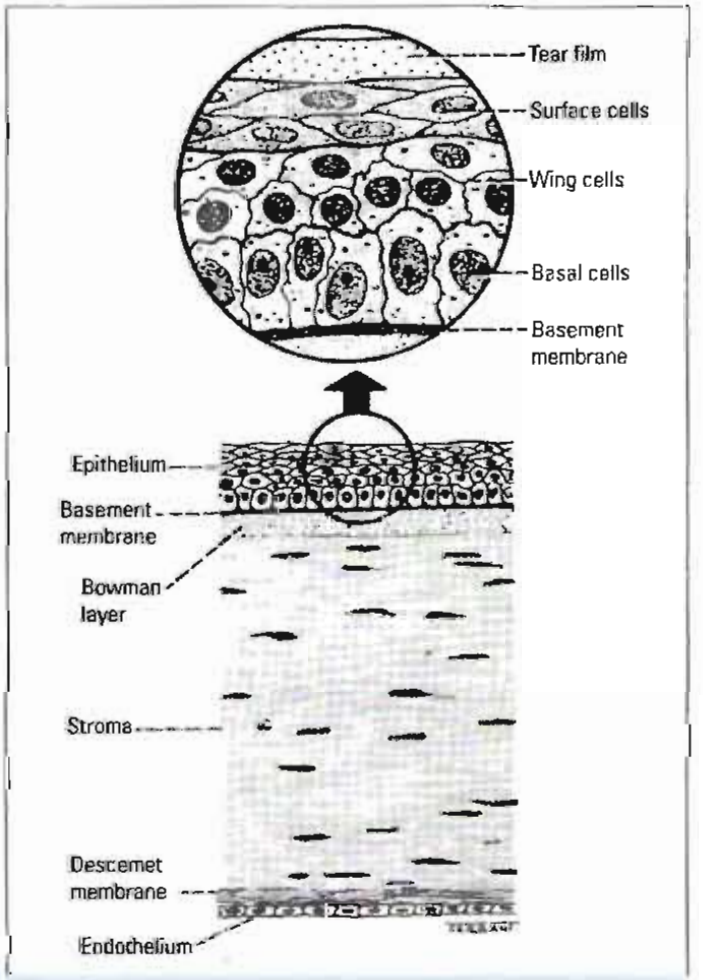

Fig. 5.1
Anatomy of the cornea

NB: The cornea is richly supplied by sensory nerve endings via the first division of the trigeminal nerve. There is a subepithelial and a stromal plexus of nerves. In eyes with corneal abrasions or bullous keratopathy, the direct stimulation of bare nerve endings causes pain, lacrimation and photophobia. Corneal oedema causes diffraction and symptoms of haloes around lights.

Slit-lamp biomicroscopy

It is important to systematically detect clinical signs with regard to position, depth and size by slit-lamp biomicroscopy as follows (Fig. 5.2):

1. **Direct illumination** with diffuse light is used to detect gross abnormalities.
   - A narrow obliquely directed slit-beam to visualize a quadrilateral cross-section of the cornea.
   - Further narrowing of the beam to visualize a very thin optical section.
   - The height of the coaxial beam can be adjusted to measure the size of a lesion.
   - The orientation can be varied by rotating the lamp housing.
   - By passing the beam across the entire cornea the thickness and depth of corneal lesions can be determined.
   - The nature of the light emitted can be modified by the use of filters. For example, the use of a red-free filter makes red objects appear black, thereby increasing contrast when observing vascular structures or rose bengal staining. A cobalt blue filter is normally used in conjunction with fluorescein.
2. **Scleral scatter** involves decentring the slit beam laterally so that the light is incident on the limbus with the microscope focused centrally. Light is then transmitted

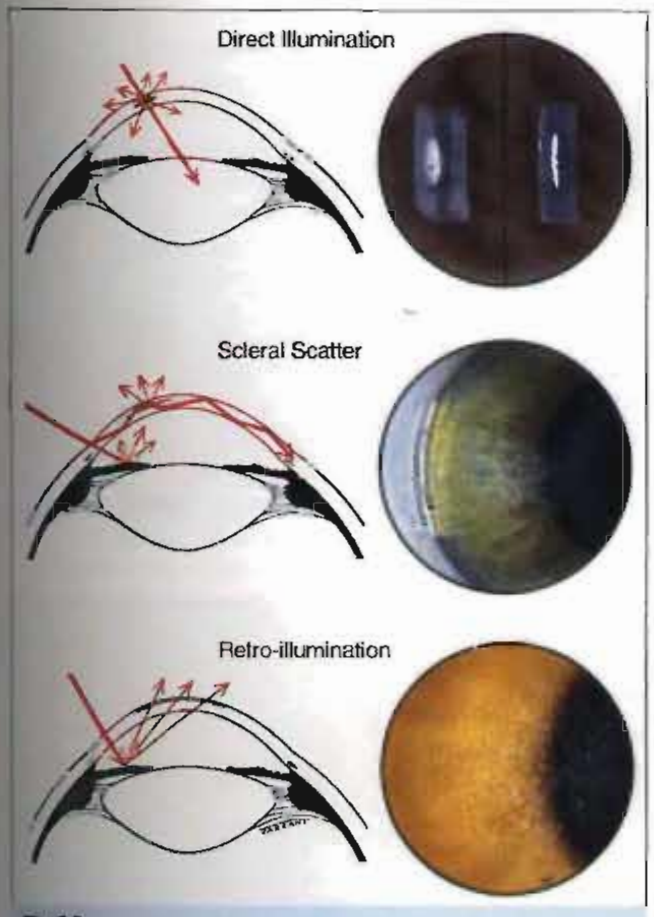

Fig. 5.2
Technique of slit-lamp biomicroscopy

within the cornea by total internal reflection, exiting at the opposite limbus. A corneal lesion will become illuminated because it scatters the internally reflected light beam. This technique is especially useful in the detection of subtle pathology.

3. **Retro-illumination** uses reflected light from the iris or fundus to illuminate the cornea. This allows the detection of fine epithelial and endothelial changes, keratic precipitates and small blood vessels.

Signs of corneal disease

Superficial lesions

1. **Punctate epithelial erosions (PEE)** are tiny, slightly depressed, epithelial defects which stain with fluorescein (Fig. 5.3) but not rose bengal. PEE are non-specific and may develop in a wide variety of keratopathies. Location may frequently indicate aetiology, for example:
   a. Superior. Vernal disease, superior limbic keratoconjunctivitis, floppy eyelids and poorly fitting contact lenses.
   b. Interpalpebral. Dry eyes, diminished corneal sensation and exposure to ultraviolet light.
   c. Inferior. Lower lid margin disease, corneal exposure, rosacea, toxicity from drops and self-induced.

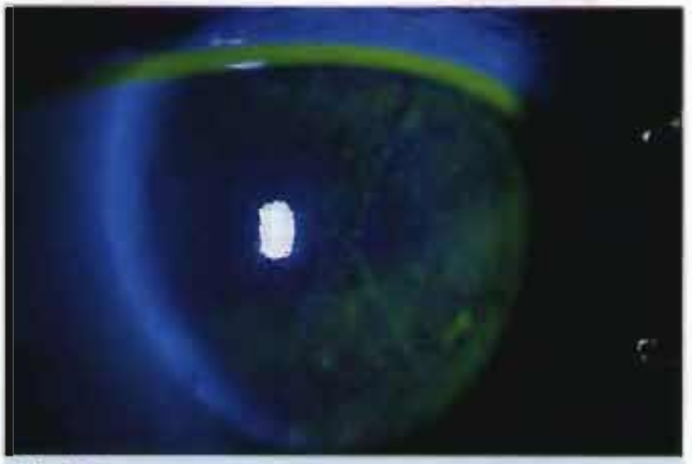

Fig. 5.3
Punctate epithelial erosions stained with fluorescein (Courtesy of A. Bacon)

Fig. 5.4
Punctate epithelial keratitis

2. **Punctate epithelial keratitis (PEK)** is the hallmark of viral infections. It is characterized by granular, opalescent, swollen epithelial cells, visible unstained (Fig. 5.4), which stain well with rose bengal but poorly with fluorescein.
3. **Epithelial oedema** is a sign of endothelial decompensation or severe, acute elevation of intraocular pressure. It is characterized by loss of normal corneal lustre (Fig. 5.5) and, if severe, may be associated with vesicles and bullae (Fig. 5.6).
4. **Filaments**
   a. Signs
   - Small, comma-shaped mucus strands lined with epithelium, attached at one end to the corneal surface (*see* Fig. 3.5); the unattached end moves with each blink. Grey subepithelial opacities may be seen at the site of attachments.
   - They stain well with rose bengal (*see* Fig. 3.5) but not fluorescein, since fluorescein remains extracellular while rose bengal stains dead and degenerating cells and mucus.

   b. Causes. Keratoconjunctivitis sicca, superior limbic keratoconjunctivitis, recurrent erosion syndrome, eye patching,

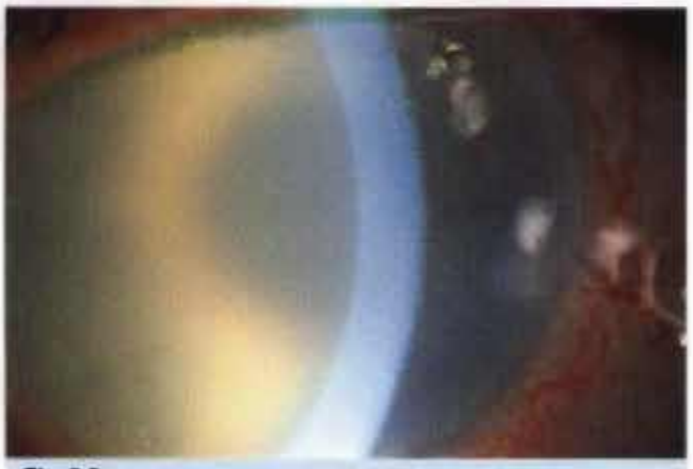

Fig. 5.5
Corneal epithelial oedema

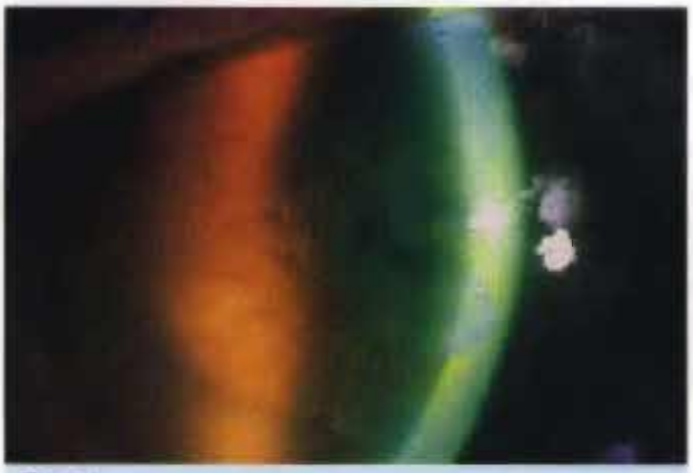

Fig. 5.6
Corneal epithelial vesicles and small bullae

corneal exposure, diminished corneal sensation, herpes zoster ophthalmicus, midbrain strokes and essential blepharospasm.

5. **Pannus** is an inflammatory or degenerative sub-epithelial ingrowth of fibrovascular tissue from the limbus. A progressive pannus is characterized by infiltration extending beyond the ingrowing vessels (Fig. 5.7). In a regressive pannus the vessels extend beyond the infiltrate.

Stromal lesions

1. **Infiltrates** are focal areas of active stromal inflammation composed of accumulations of leucocytes and cellular debris.
   a. Signs
   - Focal, granular, grey-white opacities usually within the anterior stroma and usually associated with limbal or conjunctival hyperaemia (Fig. 5.8).
   - Surrounding halo of less dense infiltration such that individual inflammatory cells may be discernible.

   b. Causes
   - Non-infectious (antigen sensitivity) causes include contact lens wear and marginal keratitis.
   - Infectious keratitis caused by bacteria, viruses, fungi and protozoa. The 'PEDAL' mnemonic is useful in distinguishing non-infectious from infectious infiltrates because the latter are frequently associated with Pain, Epithelial defects, Discharge, Anterior chamber reaction and a more central Location.
2. **Oedema**
   a. Signs. Optically empty spaces between stromal lamellae, associated with increased corneal thickness and variable decrease in transparency as a result of disruption of the regular arrangement (Fig. 5.9).
   b. Causes. Disciform keratitis, keratoconus, Fuchs dystrophy and surgical damage to the corneal endothelium.
3. **Vascularization** occurs in a wide variety of corneal disorders. Corneal blood vessels visible at the slit-lamp are invariably venous (Fig. 5.10). The arterial feeding vessels are difficult to see without fluorescein angiography. Deep vessels are derived from the anterior ciliary vessels and run

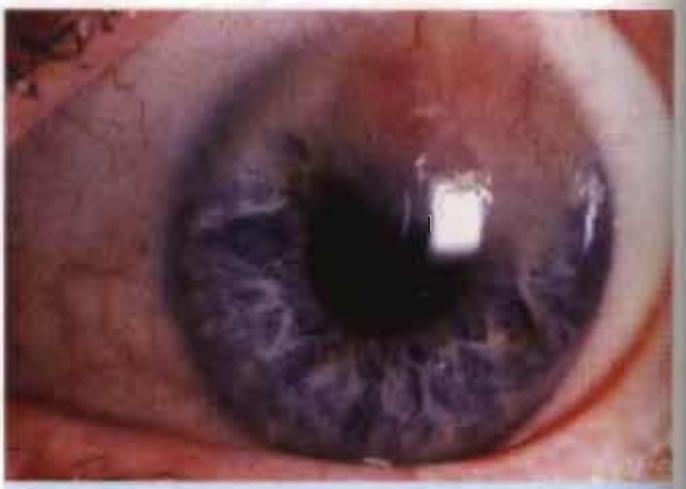

Fig. 5.7
Pannus

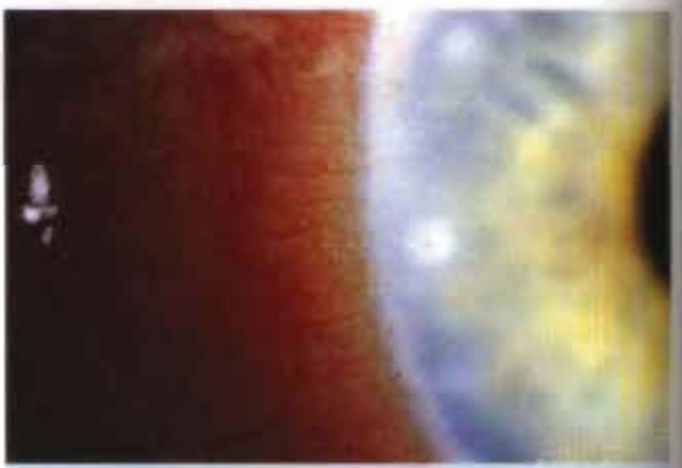

Fig. 5.8
Anterior stromal infiltrates

Fig. 5.9
Stromal corneal oedema

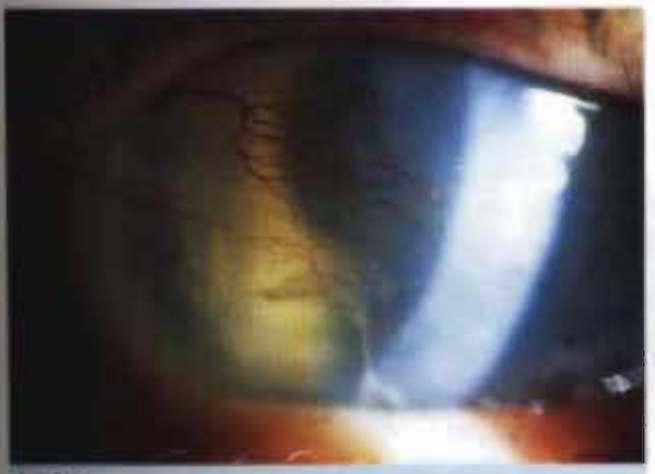

Fig. 5.10
Stromal vascularization

a straight radial course, disappearing at the limbus, unlike wavy superficial vessels which can be traced beyond the limbus. When non-perfused, deep vessels appear as 'ghost vessels', best detected by retroillumination.

Lesions of Descemet membrane

1. **Breaks** (Fig. 5.11) may occur as a result of corneal enlargement, birth trauma and keratoconus and result in acute influx of aqueous into the corneal stroma.
2. **Folds** (striate keratopathy) (Fig. 5.12) may be caused by surgical trauma, ocular hypotony, stromal inflammation and oedema.

Documentation of clinical signs

Frontal and slit views of the cornea are drawn and details added as follows (Fig. 5.13):

1. **Opacities** such as scars and degenerations are drawn in *black*.
2. **Epithelial oedema** is represented by *fine blue circles*, stromal oedema as *blue shading* and folds in Descemet membrane as *wavy blue lines*.
3. **Hypopyon** is shown in *yellow*.

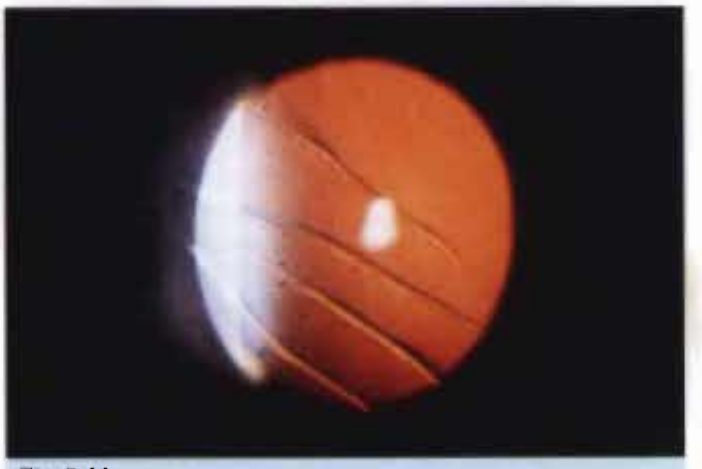

Fig. 5.11
Breaks in Descemet membrane (Courtesy of C. Barry)

Fig. 5.12
Folds in Descemet membrane

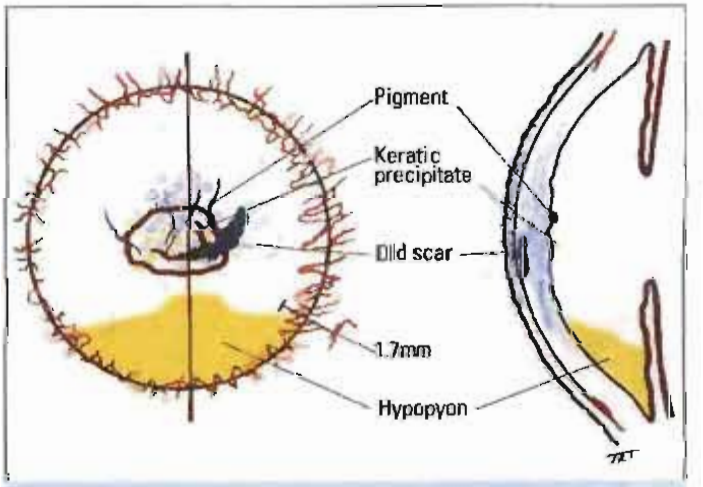

Fig. 5.13
Documentation of corneal lesions

4. **Blood vessels** are then added in *red*. Superficial vessels are wavy lines that begin outside the limbus and deep vessels are straight lines that begin at the limbus.
5. **Pigment** such as iron rings and Krukenberg spindle are shown in *brown*.

Special investigations

Optical methods

1. **Pachymetry** involves measurement of corneal thickness, which is an indirect indication of the integrity of the corneal endothelium. The thickness of the cornea is greatest at the limbus, where it ranges from 0.7 to 0.9 mm. Normal central corneal thickness is 0.49–0.56 mm; readings of 0.6 mm or more are suggestive of endothelial disease.
2. **Specular microscopy** involves photography of the corneal endothelium and subsequent analysis of cellular characteristics such as size, shape, density and distribution (Fig. 5.14). The normal endothelial cell is a regular hexagon. The normal cell density is about 3000 cells per mm^2; counts of below 1000 mm^2 are associated with a significant risk of endothelial decompensation.
3. **Keratometry** involves measurement of the curvature of the axial 2–3 mm of the anterior corneal surface.
   a. Optical principles
   - The cornea acts as a convex mirror with fixed curvatures in each meridian.
   - This allows the positions of two vertical and two horizontal points projected by the instrument to be reflected off the corneal surface. The radius is then measured in millimetres and converted to dioptres.

   b. Limitations
   - The assumption that the cornea is a sphero-cylindrical surface with a single radius of curvature in each meridian, and with major and minor axes at 90° to each other.
   - Keratometry measures only four points approximately 3 mm apart and provides no information about the cornea central or peripheral to the points measured.
   - Mild corneal surface irregularities can cause mire distortion that compromise accuracy. Keratometry is therefore of limited use for measuring corneas that are not sphero-cylindrical, as frequently occurs in refractive surgery, keratoconus and several other corneal abnormalities.
4. **Corneal topography** with computerized videokeratoscopy provides a colour-coded map of the corneal surface. The dioptric powers of the steepest and flattest meridia and their axes are also calculated and displayed.
   a. Indications
   - To quantify irregular astigmatism and corneal warpage associated with contact lens wear.
   - To diagnose early keratoconus. While advanced keratoconus is easy to diagnose, early or subclinical cases pose a diagnostic challenge.
   - To evaluate postoperative changes in corneal shape after refractive surgery, corneal grafting or cataract extraction.

   b. Scales
   - Absolute scales have fixed end-points and each individual colour represents a specific dioptric power interval. Most normal corneas remain within the yellow–green spectrum of the scale (Fig. 5.15). An absolute scale should always be used to facilitate comparison over time and between patients.
   - Relative (normalized) scales are not fixed and vary according to the dioptric range of the individual cornea (Fig. 5.16). It is very important to look carefully at the scale before attempting to interpret the map.

   c. Interpretation can be acquired only by practice. Important questions to be answered are:
   - What scale does the map show?
   - Is the scale appropriate?
   - Is the map reliable?
   - What is the position of the pupil in relation to the curvature pattern display?

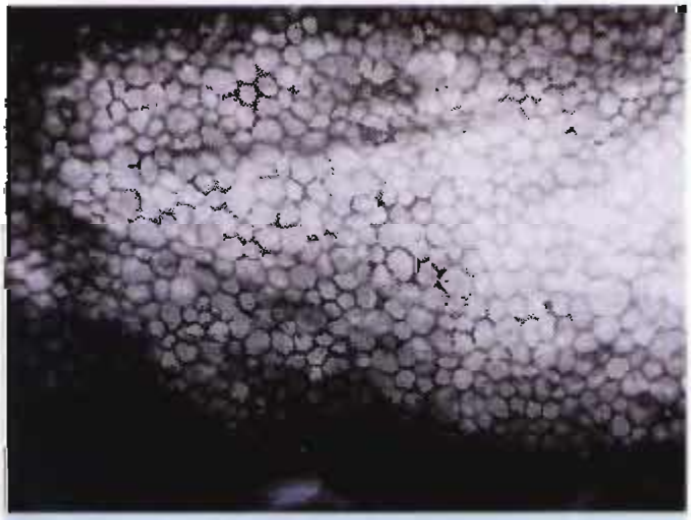

Fig. 5.14
Appearance of normal corneal endothelial cells on specular microscopy

Microbiological investigations

1. **Corneal scrapings** to obtain specimens are made with a Kimura spatula, bent tip of a 21-gauge hypodermic needle or a no. 15 blade. After the instillation of a topical preservative-free anaesthetic, the margins and base of the lesion, usually an ulcer, are gently but firmly scraped under slit-lamp visualization. Contact lens wearers should have their contact lenses and cases sent for microbiological investigation. The material is plated on to glass slides for Gram staining and on to the following culture media as appropriate:
   a. ***Blood agar*** for most bacteria and fungi.
   b. ***Thioglycolate broth*** for most bacteria.
   c. ***Chocolate agar*** for *Neisseria* and *Haemophilus*.
   d. ***Sabouraud agar*** for fungi; this is incubated at room temperature as well as at 37°C.

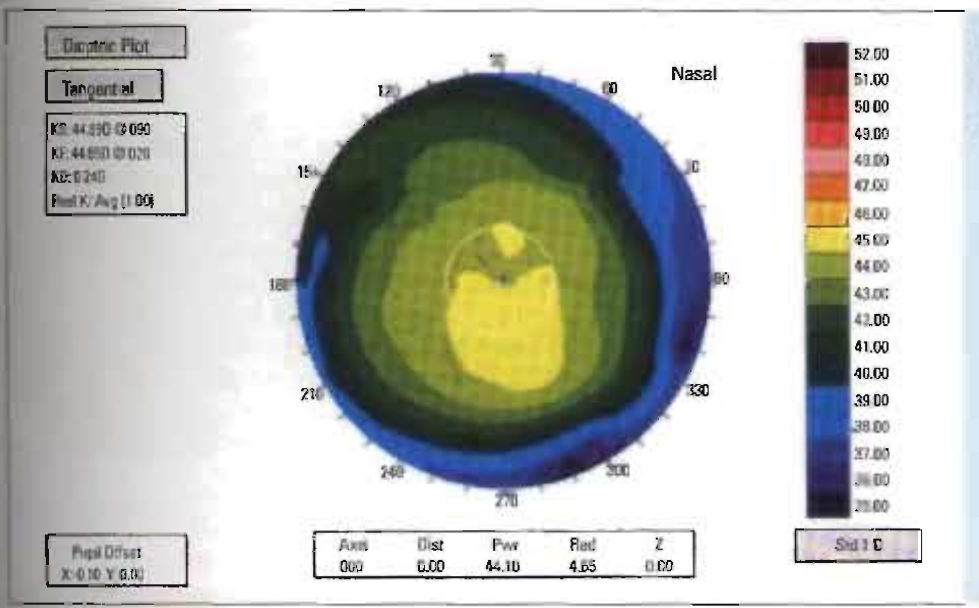

Fig. 5.15
Corneal map showing a normal spherical cornea in an absolute scale ranging from **34** to **54** D with 1 D intervals (Courtesy of E Morris)

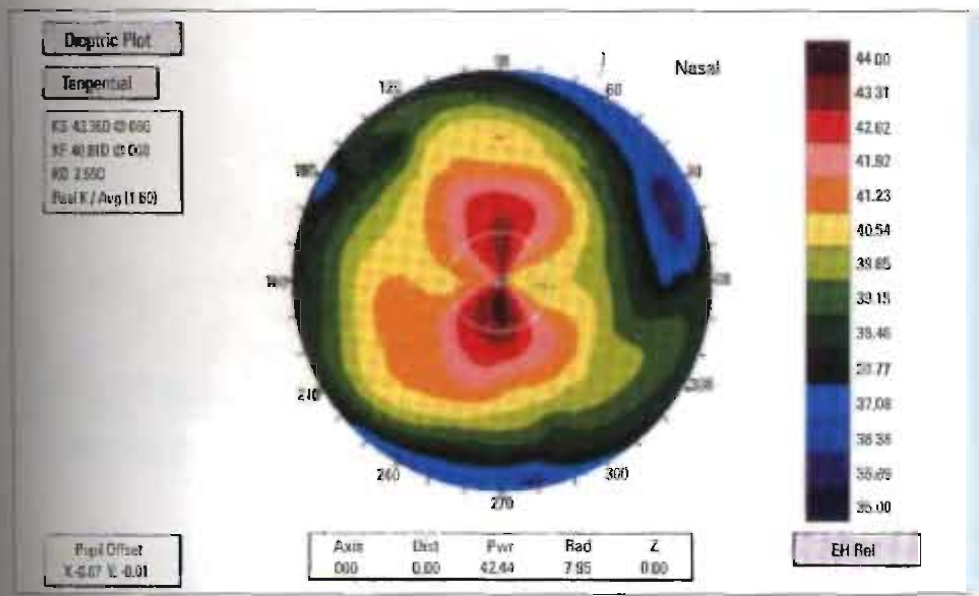

Fig. 5.16
A relative scale of a normal cornea with 3.5 D of with-the-rule astigmatism showing a typical bow-tie pattern (Courtesy of E. Morris)

e. ***Brain–heart infusion broth*** for fungi that fail to grow on Sabouraud agar.
f. ***Non-nutrient agar*** on plates preseeded with an *E. coli* culture for acanthamoeba.
g. ***Buffered charcoal–yeast extract agar*** for acanthamoeba.

N.B. Culture media should be at room temperature before inoculation.

2. **Corneal biopsy** can be performed either with a trephine or by free lamellar dissection using a sharp blade. The following are the main indications:
   - Keratitis with negative or non-contributory scrapings and cultures.
   - A corneal infiltrate that is too deep to be reached by simple scraping.
   - To diagnose problematic corneal diseases, such as rare dystrophies or systemic genetic metabolic storage disorders with corneal manifestations.

Principles of management

Control of infection and inflammation

1. **Antimicrobial agents** should be used for corneal infections as soon as preliminary investigations have been completed. Collagen shields may be useful in helping drug delivery. The shield is shaped like a contact lens and is packed in a dehydrated form which requires rehydration before application.
2. **Topical steroids** are used to suppress inflammation and limit scarring, although injudicious use may promote microbial growth. They may also suppress corneal repair, promote ulceration–perforation and are contraindicated in active herpes simplex epithelial disease.
3. **Systemic immunosuppressive agents** may be useful in certain forms of severe peripheral corneal ulceration and melting associated with systemic connective tissue disorders.

Promotion of re-epithelialization

In eyes with a thin stroma it is important to promote re-epithelialization because thinning seldom progresses if the epithelium is intact. The following are the main methods of promoting re-epithelialization:

1. **Lubrication** with artificial tears and ointments, which should not contain potentially toxic (benzalkonium) or sensitizing (thiomersal) preservatives.
2. **Eyelid closure** is particularly useful in exposure and neurotrophic keratopathies as well as in eyes with persistent epithelial defects. It can be achieved by one of the following methods:
   - Taping the lids temporarily with Blenderm or Transpore.
   - Botulinum toxin injection into the levator muscle to induce a temporary ptosis.
   - Lateral tarsorrhaphy or medial canthoplasty.
3. **Bandage soft contact lenses** promote healing by mechanically protecting regenerating corneal epithelium from the constant rubbing of the eyelids.
4. **Amniotic membrane grafting** may be necessary for persistent unresponsive epithelial defects.

Other measures

1. **Tissue adhesive** (cyanoacrylate) glue may be used to limit stromal ulceration and to seal small perforations. It is first applied onto a plastic patch which is then applied to the area of thinning or perforation and a bandage contact lens inserted (*see* Fig. 5.147).
2. **Hooding** with a conjunctival (Gundersen) flap to cover the cornea if ulceration is progressive and unresponsive. This procedure is particularly suitable for chronic unilateral disease in which the prognosis for restoration of useful vision is poor.
3. **Limbal stem cell transplantation** may be required in patients with stem cell deficiency associated with a variety of corneal disorders such as chemical burns or cicatrizing conjunctivitis. The source of the donor tissue may be the fellow eye (autograft) in unilateral disease or from a living or cadaver donor (allograft) when both eyes are affected.
4. **Keratoplasty** may be required to restore corneal transparency.

Microbial keratitis

Bacterial keratitis

Predisposing factors

Bacteria capable of penetrating intact epithelium include *Neisseria gonorrhoeae* and *H. influenzae*. Other bacteria are capable of producing keratitis only after compromisation of epithelial integrity, associated with the following factors:

1. **Contact lens wear**, particularly extended-wear soft lenses, is the most common predisposing factor in patients with previously normal eyes. Meticulous lens hygiene is therefore vital. Epithelial defects commonly occur in contact lens wearers facilitating bacterial colonization, often by *Pseudomonas aeruginosa*. The diagnosis of bacterial keratitis must therefore be considered in any contact lens user with an acutely painful red eye and a white spot on the cornea.
2. **Pre-existing corneal disease** such as trauma, bullous keratopathy, exposure and diminished corneal sensation.
3. **Other factors** include chronic blepharoconjunctivitis, chronic dacryocystitis, tear film deficiency, topical steroid therapy and hypovitaminosis A.

Clinical features

1. **Presentation** is with foreign body sensation which progresses to photophobia, blurring of vision, pain, eyelid oedema and discharge. In contact lens wearers symptoms may be masked or delayed.
2. **Signs** (in chronological order)
   - Conjunctival and circumcorneal injection.
   - An epithelial defect associated with an infiltrate around the margin and base (Fig. 5.17).
   - Enlargement of the infiltrate associated with stromal oedema (Fig. 5.18).
   - Secondary sterile anterior uveitis with hypopyon (Fig. 5.19)
   - Progressive ulceration may lead to corneal perforation and bacterial endophthalmitis (Fig. 5.20).
3. **Differential diagnosis** includes fungal keratitis, acanthamoeba keratitis, stromal necrotic herpes simplex keratitis, marginal keratitis and sterile inflammatory corneal infiltrates associated with contact lens wear.

Principles of treatment

Initial treatment should be with broad-spectrum topical antibiotics because polymicrobial infections are common and an unproductive Gram stain does not exclude bacterial infection.

1. **Dual therapy** involves a combination of two fortified antibiotics to cover common Gram-positive and Gram-negative pathogens, in the form of an aminoglycoside and a cephalosporin.
2. **Monotherapy** with a fluoroquinolone (i.e. ciprofloxacin 0.3% or ofloxacin 0.3%) is easily available but may be associated with corneal toxicity from preservatives.

> ***NB:*** Both cover the majority of pathogens and bacterial resistance is encountered in only about 5% of cases. Fluoroquinolones are only moderately effective against *Strep. pneumoniae*.

Preparation of fortified antibiotics

A standard parenteral or lyophilized antibiotic preparation is combined with a compatible vehicle such that the antibiotic does not precipitate.

Fig. 5.17
Corneal stromal infiltrate in early bacterial keratitis

Fig. 5.19
Bacterial keratitis with hypopyon

Fig. 5.18
Bacterial keratitis

Fig. 5.20
Bacterial keratitis with endophthalmitis

1. **Gentamicin** 15 mg/ml (1.5%): 2 ml parenteral antibiotic (40 mg/ml) is added to 5 ml commercially available antibiotic ophthalmic solution (0.3%).
2. **Cephazolin** 50 mg/ml (5%): 500 mg parenteral antibiotic is diluted with 2.5 ml sterile water and added to 7.5 ml of preservative-free artificial tears. This is stable for 24 hours at room temperature or 96 hours if kept in a refrigerator.

NB: Potential problems with fortified antibiotics include cost, limited availability, possibly decreased sterility, short shelf-life and need for refrigeration.

Treatment regimen

1. Topical antibiotics

- Initial instillation is at hourly intervals.
- If response is favourable, frequency can be reduced to 2-hourly during waking hours.
- If progress is maintained, fortified drops can be substituted by weaker commercial preparations which are then tapered and eventually discontinued.

NB: **It is important not to confuse failure of re-epithelialization, resulting from drug toxicity, with persistent infection.**

2. **Oral ciprofloxacin** (750 mg twice daily) may be indicated for a juxtalimbal ulcer to prevent contiguous spread to the sclera. This bactericidal antibiotic is copiously secreted in the tears, and being lipid soluble also has excellent intraocular penetration.
3. **When to change antibiotics?**
   - The initial regimen should be changed only if a resistant pathogen is isolated and ulceration is progressing.
   - There is no need to change initial therapy if this has induced a favourable response, even if cultures show a resistant organism.
4. **Atropine** is used to prevent the formation of posterior synechiae and to reduce pain from ciliary spasm.
5. **Steroid therapy** is controversial.
   - The potential benefits of topical steroids in reducing stromal necrosis and scarring should be weighed

against decreased fibroblast activity and wound healing, which increase the risk of perforation.
- Steroids also have the potential to perpetuate infection and should be used with great caution when pseudomonas has been isolated.
- For these reasons steroid therapy may be initiated only when cultures become sterile and there is clear evidence of improvement, usually 7–10 days after initiation of treatment.

Causes of failure

1. **Wrong diagnosis** caused by inappropriate cultures.
   - The most common causes are unrecognized infection with herpes simplex virus, fungi, acanthamoeba and atypical mycobacteria.
   - The cultures should be repeated on special media such as Lowenstein–Jensen (mycobacteria) and non-nutrient *E. coli* seeded agar (acanthamoeba).
   - If cultures are still negative, it may be necessary to perform corneal biopsy or excisional keratoplasty.
2. **Incorrect treatment** due to inappropriate choice of antibiotics.
3. **Drug toxicity**, particularly by the frequent instillation of aminoglycosides, may cause conjunctival and corneal epithelial changes, and delay healing.

NB: Ciprofloxacin may be associated with white corneal precipitates which may also delay epithelial healing (Fig. 5.21). For this reason, the presence of increasing injection inferiorly associated with irritation despite settling of the corneal ulcer suggests the need to discontinue medication.

Fungal keratitis

Although rare, fungal infection (keratomycosis) may have devastating effects. Fungi can cause severe stromal necrosis and enter the anterior chamber by penetrating an intact Descemet membrane. Once in the anterior chamber, the infection is very difficult to control, in part due to poor penetration of antimycotic agents. The most common pathogens are filamentous fungi (*Aspergillus* and *Fusarium* spp.) and *Candida albicans*. Filamentous keratitis is most prevalent in agricultural areas and is typically preceded by ocular trauma involving organic matter such as wood or plants. Candida keratitis typically develops in association with pre-existing corneal disease or in an immunocompromised patient.

Clinical features

1. **Presentation** is with gradual onset of foreign body sensation, photophobia, blurred vision and discharge. Topical steroids enhance fungal replication and corneal invasion and are often in inappropriate use at the time of diagnosis. Progression is much slower and less painful than in bacterial infection.
2. **Signs** vary with the infectious agent.
   a. Filamentous keratitis
   - A greyish, stromal infiltrate with a 'dry' texture and indistinct margins.
   - Surrounding, satellite, feathery, finger-like lesions and immune ring infiltrates (Fig. 5.22).
   - An underlying endothelial plaque and hypopyon may be present (Fig. 5.23).

   b. Candida keratitis is characterized by a yellow-white ulcer associated with dense suppuration similar to a bacterial keratitis.

Treatment

Before instituting antimycotic therapy, corneal scraping with a surgical blade should be performed in order to reduce the fungal load and enhance penetration of antifungal agents.

1. **Topical** treatment should be for 6 weeks.
   a. Filamentous infection is treated with Natamycin 5%. Amphotericin 0.15% may be added as a second agent if necessary.
   b. Candida infection is treated with imidazole 1% or flucytosine 1%.

Fig. 5.21
Ciprofloxacin corneal precipitates

Fig. 5.22
Filamentous fungal keratitis with small surrounding infiltrates

Fig. 5.23
Filamentous fungal keratitis with hypopyon

Fig. 5.24
Anterior stromal infiltrates in acanthamoeba keratitis

2. **Systemic** antimycotics may be required for severe keratitis or endophthalmitis.
3. **Therapeutic penetrating keratoplasty** may be required in unresponsive cases.

Acanthamoeba keratitis

Acanthamoeba sp. are ubiquitous free-living protozoa found in air, soil and fresh or brackish waters. They exist in both active (trophozoite) and dormant (cystic) forms. The cystic form is highly resilient and able to survive for prolonged periods under hostile environmental conditions, including chlorinated swimming pools, hot tubs and subfreezing temperatures in freshwater lakes. Under appropriate environmental conditions, the cysts turn into trophozoites, which produce a variety of enzymes that aid tissue penetration and destruction. Humans are largely resistant, though Acanthamoeba keratitis may occur following a minor corneal abrasion. Contact lens wearers are at particular risk although the infection may be non-contact lens related. *Acanthamoeba* may coexist as an opportunistic organism, particularly in patients with herpetic keratitis.

Fig. 5.25
Perineural infiltrates in acanthamoeba keratitis

Clinical features

1. **Presentation** is with blurred vision and severe pain which is characteristically disproportionate to clinical signs.
2. **Signs** (in chronological order)
   - Limbitis, small patchy anterior stromal (Fig. 5.24) and perineural infiltrates (radial keratoneuritis) (Fig. 5.25) are seen during the first 1–4 weeks.
   - The overlying epithelium may be intact or manifest punctate or pseudo-dendritic keratitis (Fig. 5.26).
   - Gradual enlargement and coalescence of the infiltrates may form a central or paracentral ring abscess (Fig. 5.27).
   - Small white satellite lesions may develop peripheral to the ring.

Fig. 5.26
Epithelial changes and pseudo-dendrite in acanthamoeba keratitis (Courtesy of A. Ridgway)

   - Slowly progressive stromal opacification (Fig. 5.28), scleritis and ultimately descemetocele formation.
3. **Differential diagnosis** includes herpetic and fungal keratitis. Important diagnostic clues include soft contact lens wear, severe persistent pain, negative cultures for bacteria,

Fig. 5.27
Ring infiltrate in acanthamoeba keratitis (Courtesy of A. Ridgway)

Fig. 5.28
Advanced acanthamoeba keratitis (Courtesy of A. Ridgway)

fungi and viruses and lack of response to conventional antimicrobial therapy.

Investigations

1. **Staining** and microbiological examination of corneal scrapings, biopsy material and contact lenses with calcofluor white, a chemifluorescent dye with an affinity for amoebic cysts.
2. **Cultures** using either non-nutrient agar seeded with *E. coli* or buffered charcoal–yeast extract.

Treatment

1. **Topical amoebicides**
   - A combination of propamidine isethionate (0.1% Brolene) and polyhexamethylene biguanide (0.02%) drops is well tolerated, non-toxic and largely effective.
   - A combination of Brolene and neomycin or monotherapy with chlorhexidine may also give good results.
2. **Topical steroids** may be used to control persistent inflammation but should be terminated before cessation of anti-amoebal therapy.
3. **Therapeutic penetrating keratoplasty** should be avoided in inflamed eyes, but may be necessary in severe cases to preserve the globe or, when the infection has resolved, to restore corneal clarity.

Luetic interstitial keratitis

Interstitial keratitis (IK) is an inflammation of the corneal stroma without primary involvement of the epithelium or endothelium. Apart from congenital syphilis, it may be associated with a wide variety of causes.

Fig. 5.29
Non-perfused 'ghost' vessels in old interstitial keratitis

Fig. 5.30
Intrastromal corneal haemorrhage in old interstitial keratitis

Fig. 5.31
Stromal corneal scarring in old interstitial keratitis

1. **Presentation** is between 5 and 25 years with acute bilateral pain and severe blurring of vision.
2. **Signs** (in chronological order)
   - An inflamed raised sector of limbus from which deep vessels invade the corneal stroma. Associated cellular infiltration and corneal clouding obscure the outline of the vessels, resulting in the characteristic 'salmon-patch'.
   - Anterior uveitis is present but may be obscured by corneal clouding.
   - After several months the cornea begins to clear and the vessels become non-perfused (ghost vessels) (Fig. 5.29).
   - If the cornea later becomes inflamed for any reason, the vessels may refill with blood and, rarely, bleed (Fig. 5.30).
   - Healing is associated with stromal thinning, scarring and often flattening of the cornea.
   - The inactive stage is characterized by a central deep stromal scar of variable density and ghost vessels (Fig. 5.31).
3. **Treatment** of active IK is with systemic penicillin, topical steroids and cycloplegics. Ultimate corneal clarity depends on the extent of vascularization at diagnosis.

Microsporidial keratitis

Microsporidia sp. are small, ubiquitous, obligate intracellular, spore-forming protozoa which are opportunistic pathogens that cause multi-system disease primarily in immunocompromised patients.

1. **Bilateral chronic diffuse punctate epithelial keratoconjunctivitis** may occur in patients with AIDS. Mild conjunctivitis may occur without keratitis. Treatment is with topical fumagillin and oral albendazole. Highly active antiretroviral therapy (HAART) for AIDS may also be beneficial for the eyes.
2. **Unilateral deep stromal keratitis** affects immunocompetent patients and is very rare. There is no effective treatment and most cases require corneal grafting.

Infectious crystalline keratopathy

Infectious crystalline keratopathy (arborescent bacterial keratopathy) is a rare, indolent infection usually associated with long-term topical steroid therapy, particularly following penetrating keratoplasty. Other risk factors include herpes simplex and acanthamoeba keratitis. *Strep. viridans* is most commonly responsible although other bacteria and fungi have been implicated.

1. **Signs.** Slowly progressive, grey-white, branching opacities in the anterior or mid stroma with minimal inflammation (Figs 5.32, 5.33). Rarely the lesions may involve the epithelium.
2. **Treatment** is with topical antibiotics which have to be used for several weeks.

Fig. 5.32 Early infectious crystalline keratopathy (Courtesy of M. Kerr-Muir)

Fig. 5.33
Advanced infectious crystalline keratopathy (Courtesy of M. Kerr-Muir)

Viral keratitis

Herpes simplex keratitis

Basic concepts

Herpes simplex virus (HSV) is a DNA virus which infects only humans. Infection is common; up to 90% of the population are seropositive for HSV-1 antibodies, although most infections are subclinical. HSV-1 predominantly causes infection above the waist (face, lips and eyes). HSV-2 typically causes venereally acquired infection below the waist (genital herpes). Rarely HSV-2 may be transmitted to the eye through infected genital secretions, either venereally or at birth.

1. **Primary infection** usually occurs in early childhood through droplet transmission, or less frequently by direct inoculation. Due to protection bestowed by maternal antibodies, it is uncommon during the first 6 months of life. Primary infection may be subclinical or may cause mild fever, malaise and upper respiratory infection. In immunocompromised subjects the infection may become generalized and life-threatening.
2. **Recurrent disease**
   - Following primary infection, the virus travels up the axon of a sensory nerve to its ganglion (trigeminal for HSV-1 and spinal for HSV-2), where it lies in a latent state.
   - This latent state may subsequently reverse and the virus reactivates, replicates and travels down the axon of the sensory nerve to its target tissue, causing recurrent disease (genital herpes, herpes labialis and herpetic keratitis).

NB: Without prophylactic treatment (see below) the recurrence rate of herpetic keratitis is about 33% within 1 year and 66% within 2 years.

Primary ocular infection

This typically occurs in children between the ages of 6 months and 5 years, and may be associated with generalized symptoms of a viral illness. Blepharoconjunctivitis is usually benign, self-limited and, in children, may be the only manifestation.

1. **Signs**
   - Skin vesicles typically involve the lids and periorbital area (Fig. 5.34).
   - Acute, unilateral, follicular conjunctivitis associated with preauricular lymphadenopathy.
   - Secondary canalicular obstruction may ensue.
2. **Treatment** is aimed at preventing keratitis with aciclovir eye ointment five times a day for 3 weeks. However, keratitis is uncommon even without antiviral prophylaxis.

Fig. 5.34
Blepharoconjunctivitis in primary herpes simplex infection

Epithelial keratitis

Clinical features

1. **Presentation** may be at any age with mild discomfort, watering and blurring of vision.
2. **Signs** (in chronological order)
   - Opaque epithelial cells arranged in a coarse punctate or stellate pattern (Fig. 5.35).
   - Central desquamation results in a linear-branching (dendritic) ulcer (Fig. 5.36). The ends of the branches manifest a characteristically swollen appearance (terminal bulbs). The bed of the ulcer stains with fluorescein (Fig. 5.37) and the virus-laden cells at the margin of the ulcer with rose bengal (Fig. 5.38).
   - Corneal sensation is reduced.
   - Anterior stromal infiltrates subsequently appear under the ulcer, but usually resolve rapidly once the epithelium has healed.
   - Progressive centrifugal enlargement may result in a larger epithelial defect with a geographical or 'amoeboid' configuration (Fig. 5.39), especially in the context of injudicious topical steroid therapy.
   - Following healing, the epithelium may manifest persistent linear branching shapes which represent waves of healing epithelial cells. These 'pseudodendrites' eventually resolve spontaneously and should not be mistaken for persistent active infection.
3. **Differential diagnosis** of dendritic ulceration includes herpes zoster keratitis, healing corneal abrasion, soft contact lens wear, acanthamoeba keratitis and toxic keratopathies secondary to topical medication (keratitis medicamentosa).

Fig. 5.35
Early dendritic ulcer stained with fluorescein

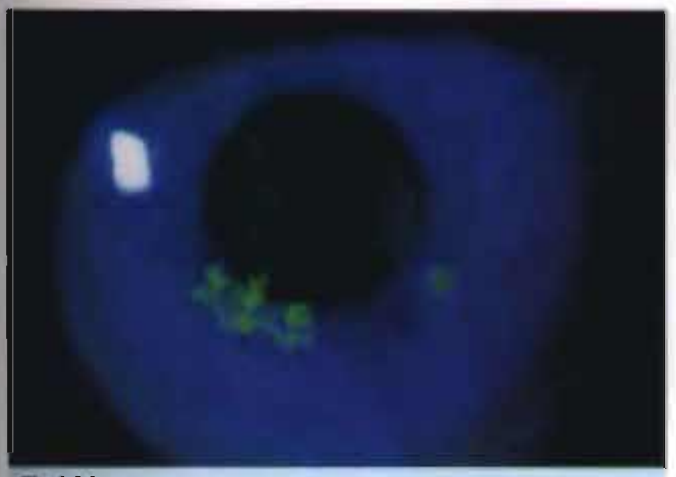

Fig. 5.36
Small dendritic ulcers stained with fluorescein

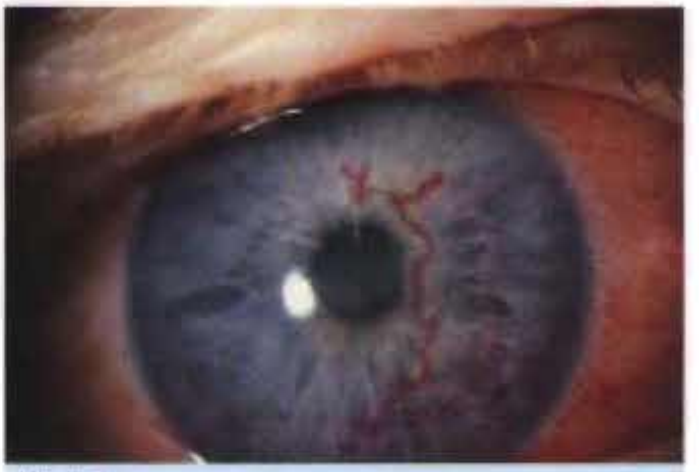

Fig. 5.38
Large dendritic ulcer stained with rose bengal

Fig. 5.37
Large dendritic ulcer stained with fluorescein

Fig. 5.39
Geographic ulcer stained with fluorescein

Treatment

1. **Topical.** Even without treatment, about 50% of active epithelial lesions heal spontaneously. The cure rate is in the order of 95% with antiviral therapy. By day 4, the lesion should start to diminish in size, and by day 10 it should have healed. After healing has occurred, medication should be quickly tapered and discontinued by day 14. When treating steroid-enhanced geographic ulcers, the steroid should be withdrawn gradually to avoid rebound worsening.
   a. ***Aciclovir*** 3% ointment (Zovirax) is used five times daily. The drug is relatively non-toxic, even when given for up to 60 days, because it acts preferentially on virus-laden epithelial cells. It is therefore suitable as antiviral cover to steroids in the management of disciform keratitis, which requires more prolonged treatment than simple dendritic ulceration (*see* below). Aciclovir penetrates intact corneal epithelium and stroma, achieving therapeutic levels in the aqueous humour, and can therefore be used to treat stromal herpetic keratitis.
   b. ***Ganciclovir*** 0.15% gel (Virgan) is a new preparation which is used five times daily and is as effective as aciclovir.
   c. ***Trifluorothymidine*** 1% drops (F3T) is used every 2 hours during the day. Like aciclovir, it heals 95% of dendritic ulcers within 2 weeks, exhibits no cross-resistance and has little tendency to produce resistant strains. It is, however, more toxic than aciclovir to the ocular surface epithelium.
2. **Debridement** may be used for dendritic but not geographic ulcers in patients who are non-compliant or allergic to antiviral agents, or if antiviral agents are not available. The corneal surface is wiped with a sterile cellulose sponge 2 mm beyond the edge of the ulcer since pathology extends well beyond the visible dendrite. The removal of the virus-laden cells protects adjacent healthy epithelium from infection and also eliminates the antigenic stimulus to stromal inflammation. Ideally, antiviral agents should be administered following debridement.

Prophylactic systemic therapy

Oral aciclovir 400 mg b.d. for 1 year reduces the rate of recurrent epithelial and stromal keratitis (*see* below) by about 45%

but this effect disappears when the drug is stopped. Prophylactic treatment should be considered mainly for patients suffering two or more attacks of epithelial keratitis annually as well as for those with previous stromal involvement.

Disciform keratitis

The exact actiology of disciform keratitis (endotheliitis) is controversial. It may be an infection of keratocytes and endothelium or an exaggerated hypersensitivity reaction to viral antigen. A past history of dendritic ulceration is not invariable.

Clinical features

1. **Presentation** is with a gradual onset of painless blurred vision which may be associated with haloes around lights.
2. **Signs**
   - A central zone of epithelial oedema overlying an area of stromal thickening which may be associated with keratic precipitates (Fig. 5.40) and folds in Descemet membrane (Fig. 5.41). Occasionally the lesion is eccentric.
   - A surrounding (Wessely) ring of stromal precipitates may be present, signifying the junction between viral antigen and host antibody (Fig. 5.42).
   - The intraocular pressure may be elevated despite only mild anterior uveitis.
   - Old healed lesions are characterized by a faint ring of stromal opacification that permanently marks the border of the previously oedematous area.
   - Corneal sensation is reduced.

Treatment

Small eccentric lesions may be observed. Large lesions involving the visual axis are treated with topical steroids with antiviral cover as follows:

- Initially the steroid and antiviral are given q.i.d.
- As improvement occurs, the strength of steroid may be reduced and antiviral administered t.i.d. In general, less than 0.25% prednisolone b.d. does not require antiviral cover.
- Steroids should be tapered over a period of several weeks, though one drop a day of a weak concentration for a prolonged period may be necessary to prevent rebound.
- Periodic attempts should be made to taper further or to stop medication altogether.

Stromal necrotic keratitis

Stromal necrotic (infiltrative) keratitis, caused by active viral invasion and tissue necrosis, is rare and may be associated with intact epithelium or may follow epithelial disease.

Clinical features

1. **Presentation** is with progressive impairment of vision associated with discomfort and pain.

Fig. 5.40
Stromal corneal oedema and keratic precipitates in herpetic disciform keratitis

Fig. 5.41
Folds in Descemet membrane in herpetic disciform keratitis

Fig. 5.42
Ring of stromal infiltrates (Wessely ring) in herpetic disciform keratitis

Fig. 5.43
Herpetic stromal necrotic keratitis

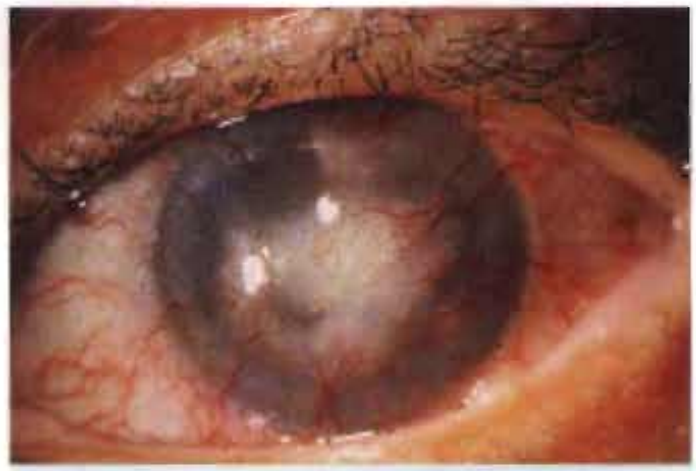

Fig. 5.44
Severe vascularization in herpetic stromal necrotic keratitis

Fig. 5.45
Corneal perforation in herpetic stromal necrotic keratitis

2. Signs

- Cheesy and necrotic stroma reminiscent of a bacterial or fungal infection, or profound interstitial opacification (Fig. 5.43).
- Associated anterior uveitis with keratic precipitates underlying the area of active stromal infiltration.
- If inappropriately treated, scarring, vascularization (Fig. 5.44), lipid keratopathy and even perforation may result (Fig. 5.45).

Treatment

- The first aim is to heal active epithelial disease with antiviral agents.
- Once the epithelium has healed, stromal inflammation may subside. However, in resistant cases with incapacitating symptoms and severe anterior uveitis, the cautious use of steroids, combined with antiviral and antibiotic cover, may be necessary to relieve symptoms and minimize scarring.
- If after 14 days, despite no evidence of active infection, the epithelium is still not healed, treatment is as for neurotrophic keratitis (*see* later).

Herpes zoster ophthalmicus

Herpes zoster (shingles) is a common disease caused by varicella zoster virus (VZV), which is morphologically identical to HSV but different antigenically and clinically. Chickenpox (varicella) and zoster are different conditions caused by the same virus. Zoster mainly affects elderly patients. After an attack of chickenpox, virus remains dormant in sensory root ganglia, perhaps arriving by retrograde spread along sensory nerves from skin lesions. Later, under the influence of largely unknown trigger factors, it reactivates and migrates back down sensory nerves to the skin and eye and causes the characteristic lesions. Virus has been cultured from these sites in the acute stage of the infection.

1. **Ocular damage** may be caused by the following independent or concomitant mechanisms.
   - Direct viral invasion may result in epithelial keratitis and conjunctivitis.
   - Secondary inflammation, occlusive vasculitis and alterations in autoimmune mechanisms may cause stromal keratitis, uveitis, scleritis and episcleritis.
   - Hypoaesthesia may result in neurotrophic keratitis.
2. **Risk of ocular involvement**
   - Approximately 15% of all cases of herpes zoster affect the ophthalmic division of the trigeminal nerve. The condition is then referred to as herpes zoster ophthalmicus (HZO), irrespective of the presence or absence of ocular involvement. Very rarely, the eye may become involved when the disease affects the maxillary nerve.
   - Involvement of the external nasal nerve (Hutchinson sign), which supplies the side of the tip of the nose, correlates significantly with subsequent development of ocular complications because it is the terminal branch of the nasociliary nerve.

- The incidence of HZO increases with age. It occurs most frequently in the sixth and seventh decades.
- In the elderly, the signs and symptoms are more severe and last longer. Patients with AIDS also tend to have more severe disease. There is, however, no correlation between ocular complications and age, sex or severity of the skin rash.

3. **Clinical phases**
   a. ***Acute***, which may totally resolve.
   b. ***Chronic***, which may persist for years.
   c. ***Relapsing***, where the acute or chronic lesions reappear, sometimes years later.

Acute phase

Systemic features

1. **An influenza-like illness** with fever, malaise, depression and headache which lasts for up to a week before the appearance of the rash.
2. **Preherpetic neuralgia** then develops over the distribution of the ophthalmic nerve and varies from a superficial itching, tingling or burning sensation to a severe deep, boring or lancing pain which is either constant or intermittent.
3. **Skin rash**
   - Cutaneous involvement starts with macules which rapidly progress through papules and vesicles to pustules, which begin to crust and scar after a few days (Fig. 5.46).
   - The lesions vary in distribution, density and severity and may involve one or more of the cutaneous branches of the ophthalmic nerve. They may be small, discrete and scattered, or large, confluent and deep with haemorrhagic bullae.
   - The rash has a dermatomal distribution and respects the midline, although inflammatory oedema may cross the midline, giving the erroneous impression of bilaterality (*see* Fig. 1.20).
   - Occasionally the rash may become generalized and the patient severely ill within 1–2 weeks. Such patients often have lymphoma, other malignancies or may be pathologically or iatrogenically immunosuppressed.

Treatment of systemic disease

1. **Systemic** treatment is with valaciclovir 1 g or famciclovir 250 mg both t.i.d. for 7 days. When administered within 72 hours of the onset of the rash antiviral therapy reduces the incidence of acute ocular complications and also has a beneficial effect on skin lesions.
2. **Topical** steroid–antibiotic skin creams such as hydrocortisone 1% with fusidic acid 2% (Fucidin-H) or with oxytetracycline 3% (Terra-Cortil) t.i.d. until the crusts have separated.

Keratitis

1. **Acute epithelial keratitis** develops in about 50% of patients within 2 days of the onset of the rash and resolves spontaneously a few days later. It is characterized by small, fine, dendritic or stellate lesions which stain with fluorescein and rose bengal. In contrast to herpes simplex dendrites, they have tapered ends which lack bulbs (Fig. 5.47).
2. **Nummular keratitis** may follow, usually about 10 days after the onset of the rash. It is characterized by multiple fine granular subepithelial deposits, surrounded by a halo of stromal haze (Fig. 5.48). They may resolve without trace or become indolent with chronic cellular and lipid infiltration, pannus, scarring, thinning and faceting. The lesions fade in response to topical steroids but recur if treatment is discontinued prematurely.
3. **Disciform keratitis** develops in about 5% of cases, 3 weeks after the onset of the rash. It is usually axial and is almost always preceded by nummular keratitis. If untreated with topical steroids, it almost invariably becomes chronic.

Fig. 5.46
Eyelid involvement in herpes zoster ophthalmicus

Fig. 5.47
Dendritic epithelial lesion in herpes zoster ophthalmicus

Fig. 5.48
Nummular keratitis in herpes zoster ophthalmicus

Other ocular complications

1. **Conjunctivitis** is common and always associated with lid margin vesicles.
2. **Episcleritis**, occurring at the onset of the rash, may be unnoticed by overlying conjunctivitis and usually resolves spontaneously.
3. **Scleritis** and sclerokeratitis are uncommon and may develop at the end of the first week. If indolent, oral flurbiprofen (Froben) 100 mg t.i.d. may be required.
4. **Anterior uveitis** frequently results in sectoral iris atrophy (*see* Figure 10.49).

Neurological complications

1. **Cranial nerve palsies** affecting the third (most common), fourth and sixth nerves are uncommon and usually recover within 6 months.
2. **Optic neuritis** occurs in about 1:400 cases.
3. **Encephalitis** is rare and only occurs with severe infection.
4. **Contralateral hemiplegia** is also rare, usually mild and typically develops 2 months after the rash.

Chronic phase

Keratitis

1. **Nummular keratitis** may persist for months, peripheral lesions sometimes forming facets which later become vascularized and infiltrated by lipid.
2. **Disciform keratitis**, if neglected, gives rise to scarring, vascularization and lipid deposition (*see* Fig. 5.83).
3. **Neutrophic keratitis** may lead to severe ulceration, secondary bacterial infection and even perforation.
4. **Mucous plaque keratitis** develops in about 5% of cases, most commonly between the third and sixth months. It is characterized by the sudden appearance of elevated mucous plaques which stain brilliantly with rose bengal (Fig. 5.49). When they assume a dendritiform configuration they may be confused with HSV dendritic ulcers. Treatment involves a combination of topical steroids and acetylcysteine. Untreated, plaques resolve after a few months, leaving a faint diffuse corneal haze.

Other ocular complications

1. **Ptosis** may develop as a result of scarring which may also produce trichiasis, madarosis and notching of the lid margin.
2. **Mucus-secreting conjunctivitis** is a common chronic condition characterized by lipid-filled granulomata under the tarsal conjunctiva and subconjunctival scarring (Fig. 5.50).
3. **Scleritis** may become chronic and lead to patchy scleral atrophy (Fig. 5.51).
4. **Postherpetic neuralgia** may be constant or intermittent, worse at night and aggravated by touch and heat. It generally improves slowly with time, although it may lead to depression, sometimes of sufficient severity to present the danger of suicide. Treatment is with oral amitriptyline and topical capsaicin cream.

Fig. 5.49
Mucus plaques stained with rose bengal in herpes zoster ophthalmicus (Courtesy of R. Marsh)

Fig. 5.50
Lipid-filled granulomata and subconjunctival scarring in herpes zoster ophthalmicus

Fig. 5.51
Scleral atrophy and corneal scarring in herpes zoster ophthalmicus

Relapsing phase

Relapsing lesions may reappear even 10 years after acute disease. They may be precipitated by the sudden withdrawal or reduction of topical steroids. The most common lesions include episcleritis, scleritis, iritis, glaucoma and nummular, disciform and mucous plaque keratitis, all of which may appear as isolated lesions because the initial attack of HZO may have been undiagnosed or forgotten.

Thygeson superficial punctate keratitis

Thygeson disease is an uncommon, bilateral, recurrent condition of unknown aetiology. Because a viral cause is suspected it is included in this section.

1. **Presentation** is with ocular irritation and watering.
2. **Signs.** Round or oval conglomerates of distinct, granular, greyish, elevated, punctate epithelial lesions (Fig. 5.52). A mild subepithelial haze may be present, especially if topical antiviral agents have been used.

NB: The conjunctiva is uninvolved.

3. **Treatment** is aimed at relieving symptoms.
   - Lubricants may suffice in mild cases.
   - Topical steroids are effective but may prolong the course of the disease.
   - Bandage contact lenses should be considered in severe cases.

Peripheral corneal disorders

Dellen

Dellen is caused by localized tear film instability which may be idiopathic or secondary to raised limbal lesions or rigid contact lens wear. It is usually innocuous and transient.

1. **Signs.** Localized, saucer-like thinning of the peripheral cornea, with dehydration of the corneal stroma and compaction of its lamellae (Fig. 5.53).
2. **Treatment** involves eliminating causative pathology and promoting corneal rehydration by padding and topical lubricants.

Marginal keratitis

Marginal keratitis (catarrhal ulcer) is caused by hypersensitivity to staphylococcal exotoxins and is therefore frequently associated with chronic staphylococcal blepharitis (*see* Chapter 1).

1. **Presentation** is in adult life with mild irritation and discomfort.
2. **Signs** (in chronological order)

Fig. 5.52
Thygeson superficial punctate keratitis

Fig. 5.53
Corneal dellen

Fig. 5.54
Early marginal keratitis

Fig. 5.55
Severe marginal keratitis stained with fluorescein

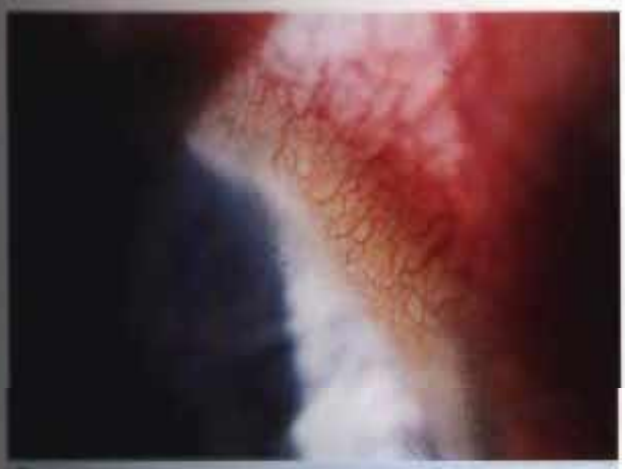

Fig. 5.56
Bridging blood vessels in marginal keratitis

- A subepithelial marginal infiltrate separated from the limbus by a clear zone (Fig. 5.54).
- Circumferential spread accompanied by breakdown of the overlying epithelium, giving rise to a fluorescein-staining ulcer (Fig. 5.55).
- Within a few days blood vessels bridge the clear corneal zone and resolution occurs (Fig. 5.56).

3. **Treatment** is with a short course of topical steroids.

> ***NB:*** Associated staphylococcal blepharitis should also be treated.

Rosacea keratitis

Acne rosacea is a common, chronic, progressive condition of unknown aetiology involving facial skin and the eyes (*see* Chapter 20). The severity of ocular involvement ranges from mild eyelid telangiectasia to corneal perforation. The extent of ocular involvement is unrelated to the severity of cutaneous disease and is often more symptomatic than clinical signs would suggest. Rosacea may therefore be missed if the face is not examined in patients with non-specific ocular symptoms.

Clinical features

1. **Presentation** is with non-specific irritation, burning, tearing and redness.
2. **Signs** (in chronological order)
   - Inferior PEE.
   - Marginal keratitis and peripheral neovascularization, especially involving the inferonasal and inferotemporal cornea (Fig. 5.57).
   - Corneal thinning may occur in severe cases (Fig. 5.58).
   - Perforation may occur as a result of severe peripheral or central melting, which may be precipitated by the excessive use of topical steroids.
3. **Other manifestations**
   a. Eyelid involvement includes lid margin telangiectasia, intractable posterior blepharitis and recurrent meibomian cysts.

Fig. 5.57
Peripheral corneal vascularization and subepithelial infiltration in rosacea keratitis

Fig. 5.58
Corneal thinning in rosacea keratitis

Fig. 5.59
Conjunctival hyperaemia in acne rosacea

*b. **Conjunctival*** hyperaemia, especially bulbar is common (Fig. 5.59). Other rare findings include cicatricial conjunctivitis, granulomas and phlyctenulosis.

*c. **Miscellaneous*** problems include episcleritis and tear film dysfunction.

Treatment

1. **Topical**
   *a. **Fluorometholone*** as a short-term measure.
   *b. **Fusidic acid*** ointment b.d. for 6 weeks.
   *c. **Lubricants*** to control tear film dysfunction.
2. **Systemic** treatment with one of the following antibiotics should be for 6–12 weeks.
   *a. **Oxytetracycline*** 500 mg b.d. The therapeutic effect is not related to antibacterial action. Although tetracycline suppresses but does not cure the disease, improvement usually lasts for 6 months after cessation of therapy.
   *b. **Doxycycline*** 100 mg once daily is an alternative but, unlike tetracycline, it should be taken in the middle of a meal to prevent gastrointestinal upset.

Fig. 5.60
Yellow dental discoloration and hypoplasia due to systemic tetracycline

NB: Systemic tetracyclines should not be used in children under the age of 12 years or in pregnant or breast-feeding women because the antibiotic is deposited in growing bone and teeth (being bound to calcium), and may cause dental staining and hypoplasia (Fig. 5.60).

*c. **Erythromycin*** 500 mg b.d. if tetracycline is contra-indicated.

Phlyctenulosis

Phlyctenulosis is caused by a non-specific delayed hypersensitivity reaction to bacterial antigens. Although commonly self-limiting the disease may rarely be severe and even blinding.

1. **Presentation** is usually in childhood with photophobia, lacrimation and blepharospasm.
2. **Signs.** A small, pinkish-white, limbal nodule associated with hyperaemia (Fig. 5.61) which may either resolve spontaneously or extend onto the cornea. A healed

Fig. 5.61
Limbal phlycten

corneal phlycten usually leaves a triangular limbal-based scar.

3. **Treatment** is with a short course of topical steroids. Associated chronic staphylococcal blepharitis, which is frequent, should also be treated.

Terrien marginal degeneration

Terrien disease is an uncommon, idiopathic, non-inflammatory thinning of the peripheral cornea. About 75% of affected patients are males and the condition is usually bilateral, although involvement may be asymmetrical.

1. **Presentation** is usually after the fourth decade with initially asymptomatic peripheral corneal lesions.
2. **Signs** (in chronological order)
   - Fine, yellow-white, punctate stromal opacities frequently associated with mild superficial vascularization usually start superiorly, spread circumferentially and are separated from the limbus by a clear zone (Fig. 5.62). On cursory examination they may resemble arcus senilis. This stage is usually asymptomatic and progression is extremely slow.

Fig. 5.62
Early Terrien marginal degeneration

Fig. 5.63
Peripheral corneal thinning in Terrien marginal degeneration

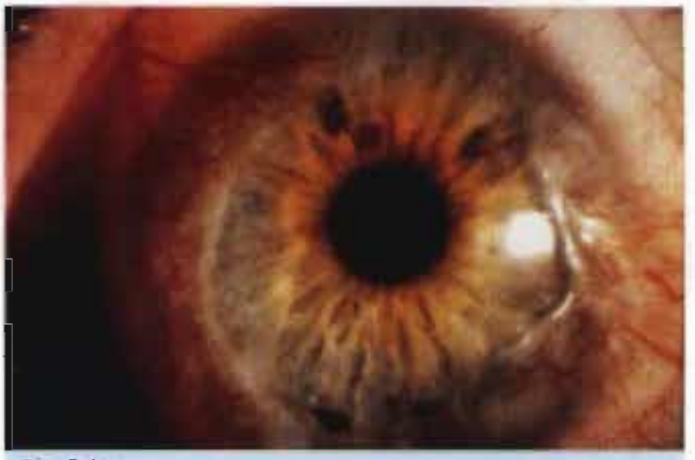

Fig. 5.64
Pseudopterygia in Terrien marginal degeneration

   - Progressive circumferential thinning results in a peripheral gutter, the outer slope of which shelves gradually, while the central part rises sharply (Fig. 5.63).
   - The floor becomes vascularized but the epithelium remains intact.
   - Gradual visual deterioration occurs as a result of increasing corneal astigmatism.
   - A few patients develop recurrent episodes of disabling pain and inflammation.
   - Pseudopterygia may develop in long-standing cases at positions other than the 9 o'clock and 3 o'clock meridia (Fig. 5.64).
3. **Treatment** of significant astigmatism is primarily with gas-permeable scleral contact lenses. While surgery involving crescent-shaped excision of the gutter with suturing of the 'healthier' margins is possible, the results are not ideal and contact lenses are usually necessary to achieve best acuity.

Mooren ulcer

Mooren ulcer is a rare but serious condition probably caused by an autoimmune response to corneal stromal antigens.

Classification

Based on clinical features, fluorescein angiographic findings and response to treatment, the following three distinct types are recognized:

1. **Unilateral ulceration** primarily affects elderly white people, usually female.
   *a. **Signs.*** Extremely painful, progressive ulceration associated with obliteration of the superficial juxtalimbal vascular plexus.
   *b. **Treatment*** is difficult as the response to both topical and systemic immunotherapy is poor. The results of corneal grafting are also unsatisfactory, with recurrence of ulceration in the graft.

2. **Bilateral aggressive ulceration** occurs primarily in young males of Indian origin. It is less painful than the unilateral type.
   a. Signs. Progressive circumferential ulceration with late centripetal spread. Fluorescein angiography shows neovascularization with leakage extending into the base of the ulcer.
   b. Treatment is initially with intravenous methylprednisolone followed by topical and systemic steroids or cytotoxic agents. Topical and systemic cyclosporin may also have a role.
3. **Bilateral indolent ulceration** usually affects middle-aged malnourished patients of Indian origin.
   a. Signs. Uncomfortable progressive peripheral guttering with minimal inflammatory response which frequently resolves spontaneously.
   b. Treatment involves improving diet and addressing any associated infection.

Signs

Signs (in chronological order), common to all forms of Mooren ulceration are:

- Peripheral corneal infiltration 2–3mm from the limbus (Fig. 5.65).
- Crescent-shaped corneal ulceration characterized by extensive undermining of the leading edge over the infiltrates (Fig. 5.66).

Fig. 5.67
Circumferential spread of Mooren ulcer

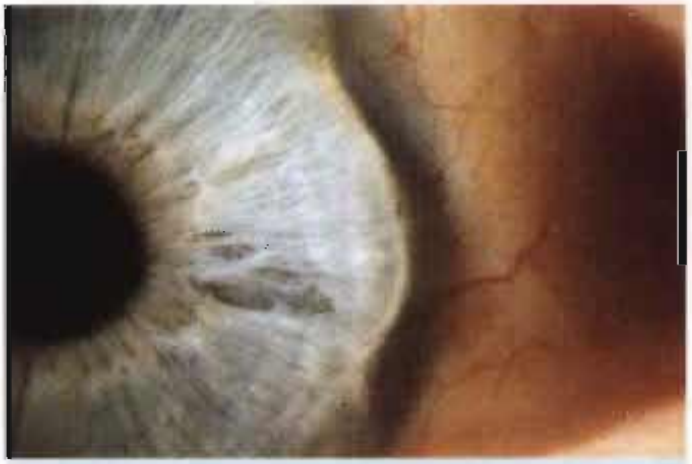

Fig. 5.65
Peripheral corneal infiltration in early Mooren ulcer

Fig. 5.68
Central spread of Mooren ulcer

Fig. 5.66
Peripheral ulceration in Mooren ulcer (Courtesy of P. Watson)

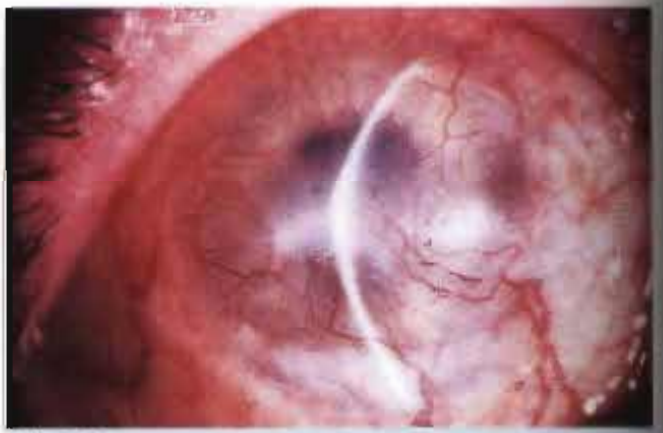

Fig. 5.69
Corneal vascularization and opacification in healed Mooren ulcer

- Circumferential (Fig. 5.67) and central spread (Fig. 5.68).
- The healing stage is characterized by thinning, vascularization and scarring (Fig. 5.69).
- Secondary cataract may form but perforation is rare and the sclera remains uninvolved.

Ulcerative keratitis in systemic disorders

Severe, persistent, peripheral corneal infiltration, ulceration or thinning unexplained by coexistent ocular disease should prompt a search for an associated systemic collagen vascular disorder. The main diseases that should be considered are: (a) rheumatoid *arthritis* and (b) *systemic vasculitides*, such as Wegener granulomatosis and polyarteritis nodosa (*see* Chapter 10). Ocular lesions may precede systemic manifestations.

Keratitis in rheumatoid arthritis

Signs

Keratitis may be primary or secondary to scleritis and may take the following forms:

1. **Sclerosing keratitis** is characterized by gradual thickening and opacification of the corneal stroma adjacent to a site of scleritis (Fig. 5.70). The pathology may extend centrally and be complicated by scarring, vascularization and lipid deposition (Fig. 5.71).
2. **Peripheral corneal thinning** (contact lens cornea) is characterized by gradual resorption of peripheral stroma, leaving the epithelium intact. The normal central cornea resembles a contact lens placed on the eye (Fig. 5.72).
3. **Acute stromal keratitis** is characterized by peripheral infiltrates associated with non-necrotizing scleritis (Fig. 5.73). Late complications include diffuse peripheral scarring and vascularization, and occasionally epithelial breakdown and stromal melting.
4. **Acute corneal melting** may occur in an area of thinned peripheral cornea of the non-inflammatory contact lens type (Fig. 5.74) or, more commonly, in association with intense inflammation at the limbus (Fig. 5.75). The central cornea may also be involved (Fig. 5.76).

Fig. 5.70
Sclerosing keratitis (Courtesy of P. Watson)

Fig. 5.71
Corneal vascularization and scarring in long-standing sclerosing keratitis

Fig. 5.72
Peripheral corneal thinning without inflammation (contact lens cornea) in rheumatoid arthritis (Courtesy of P. Watson)

Fig. 5.73
Acute stromal keratitis in rheumatoid arthritis

Fig. 5.74
Acute peripheral corneal melting without inflammation in rheumatoid arthritis (Courtesy of P. Watson)

Fig. 5.75
Acute peripheral corneal melting with inflammation in rheumatoid arthritis (Courtesy of P. Watson)

Fig. 5.76
Acute central corneal melting in rheumatoid arthritis

Fig. 5.77
Severe ulcerative keratitis in polyarteritis nodosa

Treatment

1. **Topical**
   a. ***Steroids*** may be useful in acute keratitis but should be avoided in peripheral corneal guttering and keratolysis for fear of potentiating perforation.
   b. ***Cyclosporin*** may also be beneficial.
2. **Systemic** steroids and/or cytotoxic drugs are required for scleritis.
3. **Keratoplasty** may be required either as an emergency measure to prevent perforation, or electively, to restore visual acuity.

Keratitis in systemic vasculitides

1. **Signs** (in chronological order)
   - Bilateral marginal stromal infiltrates.
   - Breakdown of the overlying epithelium.
   - Circumferentially and occasionally central spread similar to a Mooren ulcer (Fig. 5.77).
2. **Treatment** with a combination of systemic steroids and cyclophosphamide may be beneficial.

NB: Unlike Mooren ulcer the process may also extend to involve the sclera.

Corneal degenerations

Age-related degenerations

Arcus senilis

1. **Systemic implications.** Arcus senilis is the most common peripheral corneal opacity which frequently occurs without predisposing systemic conditions in elderly individuals. Occasionally arcus may be associated with familial and non-familial dyslipoproteinaemias. Hyperlipoproteinaemia, most notably type II, is frequently associated with bilateral arcus, with less common association in types III, IV and V. Unilateral arcus is a rare entity that may be associated with carotid disease or ocular hypotony.

Fig. 5.78
Arcus senilis

Arcus has also been noted in patients with Schnyder crystalline corneal dystrophy.

2 Signs (Fig. 5.78)

- Lipid stromal deposition which starts in the superior and inferior perilimbal cornea and then progresses circumferentially to form a band about 1 mm wide.
- The band is usually wider in the vertical than horizontal meridian.
- The central border of the band is diffuse; the peripheral edge is sharp and separated from the limbus by a clear zone.
- This lucid interval may occasionally undergo mild thinning (senile furrow).

Vogt limbal girdle

This is a common, innocuous, age-related finding characterized by bilateral, narrow, crescentic lines composed of chalk-like flecks running in the interpalpebral fissure along the nasal and temporal limbus (Fig. 5.79). Type 1 is separated from the limbus by a clear interval but type 2 is not.

Fig. 5.79
Type white limbal girdle

Cornea farinata

This is a visually insignificant condition characterized by minute, usually bilateral, flour-like deposits in the deep corneal stroma, most prominent centrally (Fig. 5.80).

Crocodile shagreen

This is characterized by usually asymptomatic, greyish-white, polygonal stromal opacities separated by relatively clear spaces (Fig. 5.81). The opacities most frequently involve the anterior two-thirds of the stroma (anterior crocodile shagreen), although on occasion they may be found more posteriorly (posterior crocodile shagreen).

Cornea guttata

This consists of focal accumulations of collagen on the posterior surface of Descemet membrane. The lesions appear as warts or excrescences and are secreted by abnormal

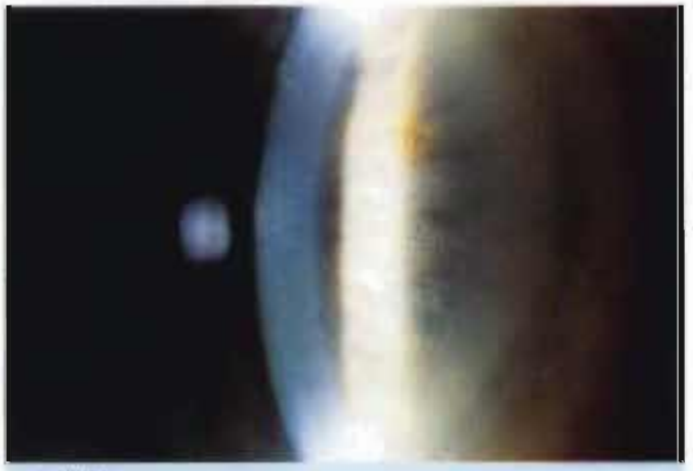

Fig. 5.80
Cornea farinata

Fig. 5.81
Crocodile shagreen

Fig. 5.82
Cornea guttata

endothelial cells. Examination by specular reflection shows tiny dark spots caused by disruption of the regular endothelial mosaic (Fig. 5.82). In more advanced cases, there is a 'beaten metal' appearance which may be associated with melanin deposition. When the lesions involve the corneal periphery, they are called Hassall–Henle bodies and are of no particular significance except as an indication of ageing. The term 'cornea guttata' is reserved for lesions involving the central cornea, which though usually innocuous, may rarely be indicative of early Fuchs endothelial dystrophy (*see* below). It is therefore important to examine the endothelium carefully prior to cataract surgery.

Lipid keratopathy

1. **Primary** lipid keratopathy is rare and occurs spontaneously. It is characterized by white or yellowish stromal deposits consisting of cholesterol, fats and phospholipids.
2. **Secondary** lipid keratopathy is much more common and is associated with previous ocular injury or disease which has resulted in corneal vascularization (Fig. 5.83). The most common causes are herpes simplex and herpes zoster disciform keratitis. It is associated with corneal vascularization and without treatment is progressive.
3. **Treatment** is primarily aimed at medical control of the underlying inflammatory disease. Other treatment options include the following:
   a. ***Argon laser photocoagulation*** to the arterial 'feeder' vessels may induce resorption of the lipid infiltrate provided they can be identified by fluorescein angiography.
   b. ***Needle point cautery*** may also be successful. It is performed by grasping a 6 mm or similar suture needle in thermal cautery forceps and applying the hot needle tip to the feeder vessels at the limbus under microscopic control.
   c. ***Penetrating keratoplasty*** may be required in advanced but quiescent disease, although vascularization, thinning and hypoaesthesia may prejudice the outcome.

Band keratopathy

Band keratopathy is a common condition characterized by the deposition of calcium salts in the anterior portion of Bowman membrane.

1. **Causes**
   a. ***Ocular*** causes, the most common, include chronic anterior uveitis (particularly in children), phthisis bulbi, silicone oil in the anterior chamber and severe chronic keratitis.
   b. ***Age-related*** band keratopathy is common and affects otherwise healthy individuals.
   c. ***Metabolic*** causes (metastatic calcification), which are rare, include increased serum calcium and phosphorus, hyperuricaemia and chronic renal failure.
   d. ***Hereditary*** causes include familial cases and ichthyosis.
2. **Signs** (in chronological order)
   - Peripheral interpalpebral calcification with clear cornea separating the sharp peripheral margins of the band from the limbus (Fig. 5.84).

Fig. 5.83
Secondary lipid keratopathy

Fig. 5.84
Mild band keratopathy

- Gradual central spread to form a band-like chalky plaque containing transparent small holes and occasionally clefts (Fig. 5.85).

Fig. 5.85
Severe band keratopathy

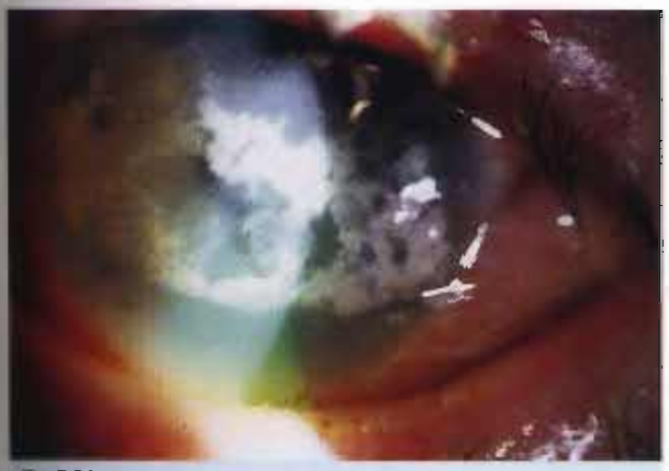

Fig. 5.86
Epithelial breakdown in longstanding band keratopathy

Fig. 5.87
Removal of corneal epithelium prior to chelation of band keratopathy

- Advanced lesions may become nodular and elevated with considerable discomfort due to epithelial breakdown (Fig. 5.86).

3. **Treatment** is indicated if vision is threatened or if the eye is uncomfortable.
   a. ***Chelation*** is simple and effective for relatively mild cases and is performed under the microscope.
      - Large chips of calcium can be manually removed with forceps.
      - The corneal epithelium overlying the opacity and any solid layer of calcification are scraped off with a No. 15 blade (Fig. 5.87).
      - A solution of sodium versenate (edetate) is applied with a cotton-tipped bud until all calcium has been removed (Fig. 5.88).
   b. ***Excimer laser keratectomy*** may be performed, if available.

NB: It is important to recognize and treat any underlying conditions to prevent recurrences.

Spheroidal degeneration

Spheroidal degeneration has many eponyms, including corneal elastosis, Labrador keratopathy, climatic droplet keratopathy and Bietti nodular dystrophy. It is a bilateral, degenerative condition of unknown cause which typically occurs in men whose working lives are spent outdoors. The main postulated predisposing factor is ultraviolet exposure, since severity correlates closely with the length of time spent outdoors. The condition is relatively innocuous although visual impairment may occur rarely.

1. **Signs** (in chronological order)
   - Small, amber-coloured granules in the superficial stroma of the peripheral interpalpebral cornea.
   - Increasing opacification, coalescence and central spread.
   - Advanced lesions are nodular and the surrounding stroma often hazy (Fig. 5.89).

Fig. 5.88
Application of sodium versenate

Fig. 5.89
Spheroidal degeneration

2. **Treatment**
   a. ***Protection against ultraviolet damage*** with sunglasses.
   b. ***Superficial keratectomy*** to improve vision.
   c. ***Lamellar keratoplasty*** may be required for visually incapacitating cases.

Salzmann nodular degeneration

Salzmann nodular degeneration occurs secondary to chronic keratitis, especially trachoma.

1. **Signs**
   - Discrete, elevated grey or blue-grey, nodular, superficial stromal opacities (Fig. 5.90).
   - The lesions are located in scarred cornea or at the edges of transparent cornea.
   - The base of a nodule may be surrounded by epithelial iron deposits.
   - Recurrent epithelial erosions may occur.
2. **Treatment** is similar to that of spheroidal degeneration.

Fig. 5.90
Salzmann nodular degeneration

Corneal dystrophies

The corneal dystrophies are a group of progressive, usually bilateral, mostly genetically determined, non-inflammatory, opacifying disorders. The age at presentation varies between the first and fourth decades depending on the relative frequency of secondary recurrent epithelial erosions and visual impairment. Based on biomicroscopic and histopathological features, corneal dystrophies are classified into (a) *epithelial*, (b) *Bowman layer*, (c) *stromal* and (d) *endothelial*. Recent advances in molecular genetics have identified the responsible gene defects for most of the dystrophies.

Epithelial dystrophies

Epithelial basement membrane dystrophy

Also known as Cogan microcystic or map-dot-fingerprint dystrophy, this is the most common dystrophy seen in clinical practice, despite which it is frequently misdiagnosed due to its variable appearance. In contrast to other dystrophies it is neither familial nor progressive.

1. **Onset** is in the second decade. About 10% of patients develop recurrent corneal erosions in the third decade. The remainder are asymptomatic throughout life. Simultaneous bilateral recurrent erosions suggest epithelial basement membrane dystrophy.

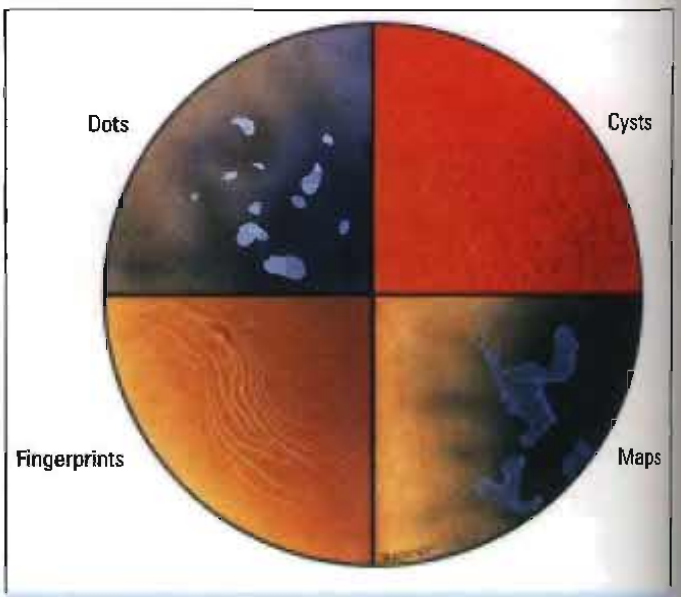

Fig. 5.91
Cogan dystrophy

2. **Signs**. The following lesions may be seen in isolation or combination and are best visualized by retroillumination or scleral scatter (Fig. 5.91).
   - Dot-like opacities (Fig. 5.92).
   - Epithelial microcysts (Fig. 5.93).
   - Subepithelial map-like patterns (Fig. 5.94).
   - Whorled fingerprint-like lines.

NB: Over time one pattern frequently changes to another and the distribution of the lesions may also vary.

3. **Histology** shows thickening of the basement membrane with deposition of fibrillary protein between the basement membrane and Bowman layer. There is also absence of hemidesmosomes of the basal epithelial cells, which is responsible for recurrent corneal erosions.
4. **Treatment** is that of recurrent corneal erosions.

Fig. 5.94
Subepithelial map-like patterns in Cogan dystrophy (Courtesy of J Talks)

Meesmann dystrophy

1. **Inheritance** is autosomal dominant (AD) with the gene locus on 12q13 or 17q12.

Fig. 5.92
Dot-like opacities in Cogan dystrophy

Fig. 5.95
Meesmann dystrophy

Fig. 5.93
Epithelial microcysts in Cogan dystrophy

2. **Onset** of this very rare dystrophy is in the first 2 years of life with ocular irritation.
3. **Signs**. Myriads of tiny intraepithelial cysts of uniform size but variable density which are maximal centrally and extend towards but do not reach the limbus, which are best seen on retroillumination (Fig. 5.95).
4. **Histology** shows irregular thickening of the corneal epithelium with numerous vacuolated suprabasal cells.
5. **Treatment** is not normally required.

Bowman layer dystrophies

Reis–Bücklers dystrophy (Bowman layer type I)

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is in early childhood with recurrent erosions.

Fig. 5.96
Reis–Bücklers dystrophy

Fig. 5.98
Schnyder dystrophy (Courtesy of K. Nischal)

3. **Signs**
   - Grey-white, fine, round and polygonal opacities in Bowman layer, most dense centrally (Fig. 5.96).
   - The changes increase in density with age, resulting in a reticular pattern due to the laying down of irregular bands of collagen replacing Bowman layer.
   - Corneal sensation is reduced and visual impairment may occur due to scarring at Bowman layer.
4. **Histology** shows that the new collagen stains blue with Masson trichrome, and Bowman layer is indistinct or absent.
5. **Treatment** is mainly by excimer laser keratectomy. Lamellar keratoplasty may be required in some cases but is associated with a high incidence of recurrence of the dystrophy on the graft, which may develop rapidly.

Thiel–Behnke dystrophy (Bowman layer type 2)

1. **Inheritance** is AD with the gene locus on 10q24.
2. **Onset** is at the end of the first decade with recurrent erosions.
3. **Signs** are similar to Reis–Bücklers dystrophy except that the opacities assume more of a honeycomb pattern (Fig. 5.97).
4. **Histology** is similar to Reis–Bücklers dystrophy.
5. **Treatment** may not be necessary because visual impairment is less than in Reis–Bücklers dystrophy.

Central Schnyder (crystalline) dystrophy

1. **Inheritance** is AD with the gene locus on 1p36–p34.1.
2. **Onset** is in the second decade with visual impairment, particularly with glare.
3. **Signs**. Central, oval area of scintillating, subepithelial 'crystalline' opacity in a generally hazy cornea (Fig. 5.98).
4. **Histology** shows deposits of phospholipid and cholesterol.
5. **Treatment** is by excimer laser keratectomy.

Stromal dystrophies

Lattice dystrophy type I (Biber–Haab–Dimmer)

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is at the end of the first decade with recurrent erosions which precede typical stromal changes. It may therefore be initially missed.

Fig. 5.97
Thiel–Behnke dystrophy

Fig. 5.99
Mild lattice dystrophy type 1

3. **Signs** (in chronological order)
   - Anterior stromal dots.
   - Progression and coalescence into fine, spidery, branching lattice lines best seen on retroillumination (Fig. 5.99).
   - Deep and outward spread sparing the periphery (Fig. 5.99).
   - Generalized haze progressively impairs vision and may obscure the lattice lines (Fig. 5.100).
4. **Histology** shows amyloid which stains with Congo Red, exhibits metachromasia with Crystal Violet and birefringence under crossed polaroids.
5. **Treatment** by penetrating or deep lamellar keratoplasty is frequently required before the sixth decade.

Lattice dystrophy type 2 (Meretoja syndrome)

1. **Inheritance** is AD with the gene locus on 9q34.
2. **Onset** is in middle age with progressive facial palsy and corneal involvement. Recurrent erosions are less frequent than in type 1 lattice.
3. **Signs.** Randomly scattered, short, fine lattice lines which are sparse, more delicate and more radially orientated (Fig. 5.101) than in type 1 lattice dystrophy.
4. **Systemic features** include progressive bilateral cranial and peripheral neuropathy, dysarthria, dry and extremely lax itchy skin, a characteristic 'mask-like' facial expression, protruding lips and pendulous ears. Amyloidosis may also involve the kidneys and heart.
5. **Histology** shows amyloid deposits in the corneal stroma and other involved sites.
6. **Treatment** by penetrating or deep lamellar keratoplasty may be required in the seventh decade but may be complicated by recurrent infections consequent to exposure keratopathy.

Lattice dystrophy type 3 and 3A

1. **Inheritance** of type 3 is presumed to be autosomal recessive (AR) and that of type 3A is AD with the gene locus on 5q31 in both.
2. **Onset** is between the fourth and sixth decades with visual impairment but recurrent erosions are uncommon.
3. **Signs**
   - Thick, ropy lines extending from limbus to limbus with minimal intervening haze (Fig. 5.102).

Fig. 5.100
Advanced lattice dystrophy type 1

Fig. 5.102
Lattice dystrophy type 3

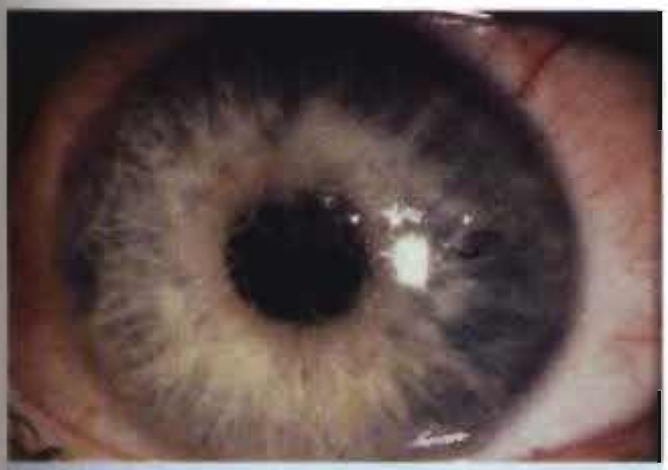

Fig. 5.101
Lattice dystrophy type 2

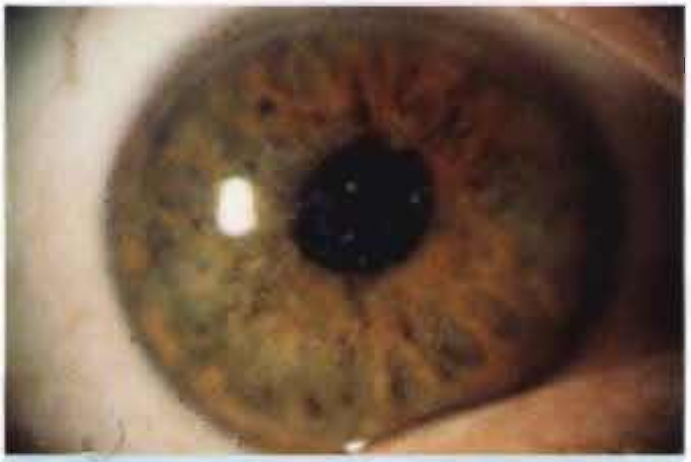

Fig. 5.103
Mild granular dystrophy (Courtesy of A. Ridgway)

- There may be gross asymmetry or the lesions may be unilateral for a time.
- Progression is rapid if the cornea is subjected to trauma, however minor.

4. **Treatment** by penetrating or deep lamellar keratoplasty is invariably required.

Granular dystrophy

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is in the first decade with recurrent erosions.
3. **Signs** (in chronological order)
   - Small, white, sharply demarcated deposits resembling crumbs or snowflakes in the central anterior stroma (Fig. 5.103).
   - Increase in number of lesions with deeper and outward spread but not reaching the limbus (Fig. 5.104).
   - Gradual confluence causing impairment of visual acuity (Fig. 5.105).
4. **Histology** shows amorphous hyaline deposits which stain bright red with Masson trichrome.
5. **Treatment** by penetrating or deep lamellar keratoplasty is usually required by the fourth decade. Superficial recurrences may require repeated excimer laser keratectomy.

Avellino dystrophy

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is in the first to second decades. Recurrent erosions are rare and, if present, mild, so that some patients may be unaware of their disease.
3. **Signs**. Superficial, fine, opacities that resemble rings, discs, stars or snowflakes, most dense centrally, resembling those seen in granular dystrophy associated with deeper linear opacities reminiscent of lattice dystrophy (Fig. 5.106).
4. **Histology** shows both hyaline and amyloid in the stroma.
5. **Treatment** is usually not required.

NB: Avellino, granular and lattice type I dystrophies are linked to a single locus on chromosome 5q and may therefore represent different clinical forms of the same entity.

Fig. 5.104
Advanced granular dystrophy (Courtesy of A. Ridgway)

Fig. 5.106
Avellino dystrophy

Fig. 5.105
Very severe granular dystrophy (Courtesy of A. Ridgway)

Fig. 5.107
Mild macular dystrophy (Courtesy of A. Ridgway)

Macular dystrophy

This is the least common stromal dystrophy in which a systemic inborn error of keratan sulphate metabolism has only corneal manifestations. It has been divided into types I, IA and II depending on the presence or absence of antigenic keratan sulphate (aKS) in the serum and cornea, though the corneal morphology is identical.

1. **Inheritance** is AR with the gene locus on 16q21.
2. **Onset** is towards the end of the first decade with gradual visual deterioration.
3. **Signs** (in chronological order)
   - Greyish-white, dense, focal, poorly delineated spots in the superficial cornea with mild diffuse stromal clouding (Fig. 5.107).
   - Increasing opacification (Fig. 5.108).
   - Eventual involvement of full-thickness stroma up to the limbus, associated with corneal thinning (Fig. 5.109).
4. **Histology** shows abnormally close packing of collagen in the corneal lamellae and abnormal aggregations of glycosaminoglycans which stain with Alcian Blue.

Fig. 5.108
Advanced macular dystrophy (Courtesy of A. Ridgway)

Fig. 5.109
Very severe macular dystrophy (Courtesy of A. Ridgway)

Fig. 5.110
Gelatinous drop-like dystrophy (Courtesy of T.A. Casey, K.W. Sharif, *Corneal Dystrophies and Degenerations*, Wolfe, 1991)

5. **Treatment** by penetrating keratoplasty is generally successful but late recurrence on the graft may occur.

Gelatinous drop-like dystrophy

This rare disorder is also known as familial subepithelial amyloidosis of the cornea.

1. **Inheritance** is AR.
2. **Onset** is in the first to second decades with severe photophobia, watering and visual impairment.
3. **Signs** (in chronological order)
   - Grey subepithelial nodules.
   - Gradual confluence, stromal involvement and increase in size giving rise to a nubbly, mulberry-like appearance (Fig. 5.110).
3. **Histology** shows subepithelial and anterior stromal accumulation of amyloid.
4. **Treatment** is with repeated superficial keratectomy because of early recurrences on corneal grafts.

Endothelial dystrophies

Fuchs endotheliai dystrophy

Fuchs endothelial dystrophy is more common in women and is associated with a slightly increased prevalence of primary open-angle glaucoma.

1. **Inheritance** may occasionally be AD although the majority are sporadic.
2. **Onset** of this slowly progressive disease is in old age.
3. **Signs** (in chronological order)
   a. ***Stage 1*** is characterized by a gradual increase of central guttata with peripheral spread and confluence, giving rise to a 'beaten-metal' appearance (Fig. 5.111).
   b. ***Stage 2*** is characterized by endothelial decompensation resulting in central stromal oedema and blurred vision, initially worse in the morning, which clears later in the

day. Epithelial oedema develops when stromal thickness has increased by about 30% (Fig. 5.112).

c. *Stage 3* is characterized by persistent epithelial oedema and results in bullae (bullous keratopathy) (Fig. 5.113) which cause pain and discomfort on rupture, due to exposure of naked nerve endings. Replacement of Bowman layer by a degenerative pannus and gradual stromal opacification supervene.

4. **Treatment**
   a. ***Hypertonicity*** of the tear film may be achieved by sodium chloride 5% drops or ointment or simple measures such as a hair dryer. This may be effective in 'dehydrating' early epithelial oedema.
   b. ***Bandage contact lenses*** provide comfort by protecting exposed nerve endings and flattening bullae.
   c. ***Penetrating keratoplasty*** has a high success rate and should not be delayed.
   d. ***Other options*** in eyes with poor visual potential include conjunctival flaps and amniotic membrane transplants.

Fig. 5.111
'Beaten-metal' appearance in early Fuchs endothelial dystrophy

Fig. 5.112
Corneal epithelial oedema in Fuchs endothelial dystrophy

Fig. 5.113
Bullous keratopathy in advanced Fuchs endothelial dystrophy

Posterior polymorphous dystrophy

This is a rare, innocuous and asymptomatic dystrophy in which corneal endothelial cells display characteristics similar to epithelium.

1. **Inheritance** is usually AD with the gene locus on chromosome 20.
2. **Onset** is at birth or soon thereafter, although is most frequently identified by chance in later life.
3. **Signs** (Fig. 5.114), which are subtle, consist of vesicular (Fig. 5.115), band-like (Fig. 5.116) or geographic endothelial patterns which may be asymmetrical.
4. **Associations** include iris membranes, peripheral anterior synechiae, ectropion uveae, corectopia and glaucoma reminiscent of iridocorneal endothelial syndrome (see Chapter 9). It has therefore been speculated that the two clinical pictures may represent points on a spectrum of

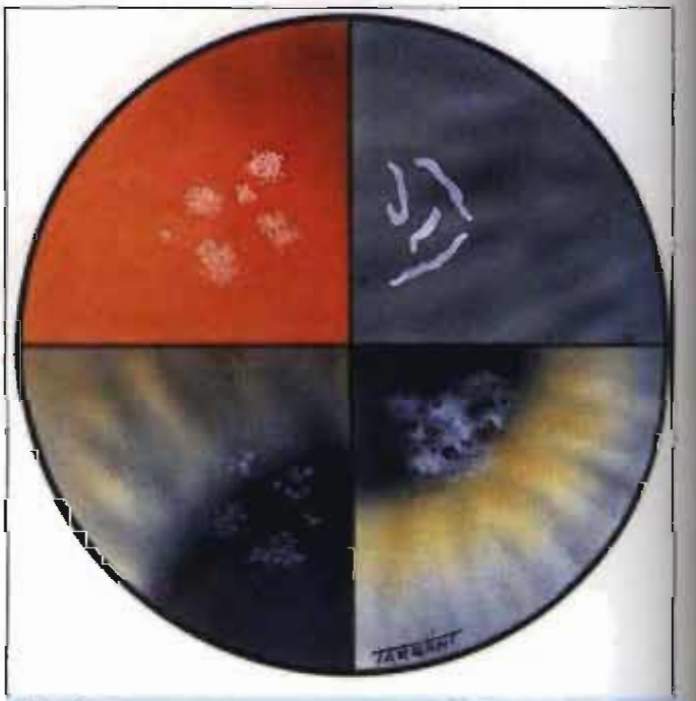

Fig. 5.114
Posterior polymorphous dystrophy

Fig. 5.115
Vesicular lesions in posterior polymorphous dystrophy

Fig. 5.116
Band-like lesion in posterior polymorphous dystrophy

one disease. There is also an association with Alport syndrome.

5. **Treatment** is not required.

Congenital hereditary endothelial dystrophy (CHED)

This is a rare dystrophy in which there is focal or generalized absence of corneal endothelium. There are two main forms, CHED1 and CHED2, the latter being more severe.

1. **Inheritance**
   - *a.* CHED1 is autosomal dominant with the gene locus on 20p11.2-q11.2.
   - *b.* CHED2 is autosomal recessive with the gene locus on 20p13.
2. **Onset** is at or shortly after birth.
3. **Signs**
   - Bilateral, symmetrical, diffuse corneal oedema.
   - Corneal appearance varies from a blue-grey, ground-glass appearance (Fig. 5.117) to total opacification.

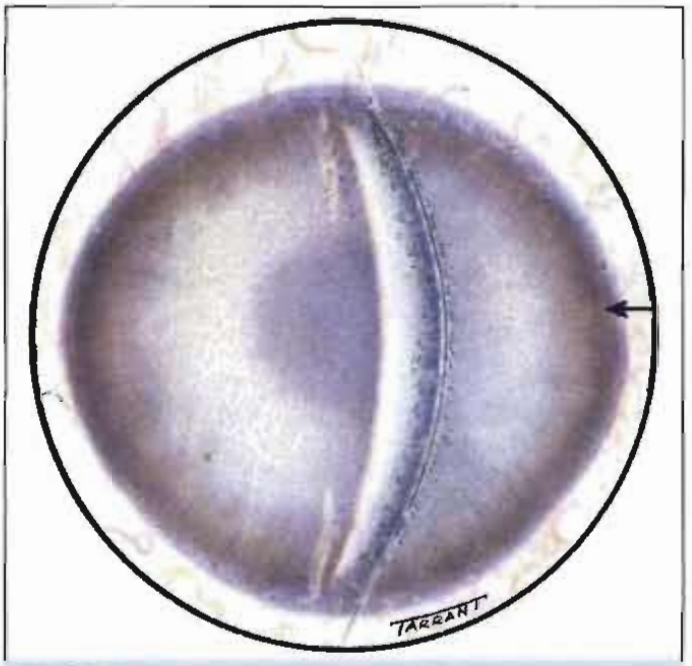

Fig. 5.117
Congenital hereditary endothelial dystrophy (Courtesy of T.A. Casey, K.W. Sharif *Corneal Dystrophies and Degenerations*, Wolfe, 1991)

   - Visual impairment is variable; acuity may surpass that expected from corneal appearance.
4. **Differential diagnosis** includes other causes of neonatal corneal opacification such as congenital glaucoma, mucopolysaccharidoses, birth trauma, rubella keratitis and sclerocornea.
5. **Treatment** by penetrating keratoplasty has a reasonable chance of success when performed early but is risky and technically more difficult than that in adults. Undue delay in surgical intervention carries the risk of dense amblyopia.

Corneal ectasias

Keratoconus

Keratoconus is a progressive disorder in which the cornea assumes an irregular conical shape. The onset is at around puberty with slow progression thereafter, though the ectasia may become stationary at any time. Both eyes are affected, if only topographically, in almost all cases. The role of heredity has not been clearly defined and most patients do not have a positive family history. Offspring appear to be affected in only about 10% of cases and AD transmission with incomplete penetrance has been proposed.

Associations

1. **Systemic disorders** include Down, Turner, Ehlers–Danlos and Marfan syndromes, atopy, osteogenesis imperfecta and mitral valve prolapse.

2. **Ocular associations** include vernal keratoconjunctivitis, blue sclera, aniridia, ectopia lentis, Leber congenital amaurosis and retinitis pigmentosa. Rigid contact lens wear and constant eye rubbing have also been proposed as predisposing factors.

Classification according to morphology

1. **Nipple cones** are characterized by small size (5 mm) and steep curvature (Fig. 5.118). The apex is central or paracentral and displaced inferonasally.
2. **Oval cones** are larger (5–6 mm), ellipsoid and commonly decentred inferotemporally (Fig. 5.119).
3. **Globus cones** are the largest (>6 mm) and may involve over 75% of the cornea (Fig. 5.120).
   In mild cases cone morphology may be indeterminate.

Fig. 5.120
Globus cone in keratoconus

Fig. 5.118
Nipple cone in keratoconus

Presentation

This is with unilateral impairment of vision due to progressive myopia and astigmatism, which subsequently becomes irregular. The patient may report frequent changes in spectacle prescription or decreased tolerance to contact lens wear. As a result of the asymmetrical nature of the condition, the fellow eye usually has normal vision with negligible astigmatism at presentation, which however, increases as the condition progresses.

Signs

The hallmark of keratoconus is central or paracentral stromal thinning, apical protrusion and irregular astigmatism. It can be graded by keratometry according to severity as mild (<48 D), moderate (48–54 D) and severe (>54 D).

Fig. 5.119
Oval cone in keratoconus (Courtesy of R. Visser)

Fig. 5.121
'Oil-droplet' reflex in keratoconus

1. **Early signs**, often subtle, can be detected as follows:
   - Direct ophthalmoscopy from a distance of one foot shows an 'oil droplet' reflex (Fig. 5.121).
   - Retinoscopy shows an irregular 'scissor' reflex.
   - Slit-lamp biomicroscopy shows very fine, vertical, deep stromal striae (Vogt lines) which disappear with external pressure on the globe (Fig. 5.122).
   - Prominent corneal nerves may also be present.
   - Keratometry shows irregular astigmatism where the principal meridia are no longer 90° apart and the mires cannot be superimposed.
   - Corneal topography is the most sensitive method for detecting very early keratoconus (Fig. 5.123).
2. **Late signs**
   - Progressive corneal thinning, to as little as one-third of normal thickness, associated with poor visual acuity resulting from marked irregular myopic astigmatism with steep keratometry (K) readings.

Fig. 5.122
Vogt striae in keratoconus

Fig. 5.124
Munson sign in keratoconus

   - Bulging of the lower lid in downgaze (Munson sign) (Fig. 5.124).
   - Epithelial iron deposits (Fleischer ring) may surround the base of the cone and are visualized best with a cobalt blue filter.
   - Stromal scarring in severe cases (Fig. 5.125).
3. **Acute hydrops** is an acute influx of aqueous into the cornea as a result of a rupture in Descemet membrane (Fig. 5.126). This causes a sudden drop in visual acuity associated with discomfort and watering. Although the break usually heals within 6–10 weeks and the corneal oedema clears, a variable amount of stromal scarring may develop. Acute episodes are initially treated with hypertonic saline and patching or a soft bandage contact lens. Healing may result in improved visual acuity as a result of scarring and flattening of the cornea. Keratoplasty should be deferred until the oedema has resolved.

Management

1. **Spectacles** in early cases to correct regular and mild irregular astigmatism.

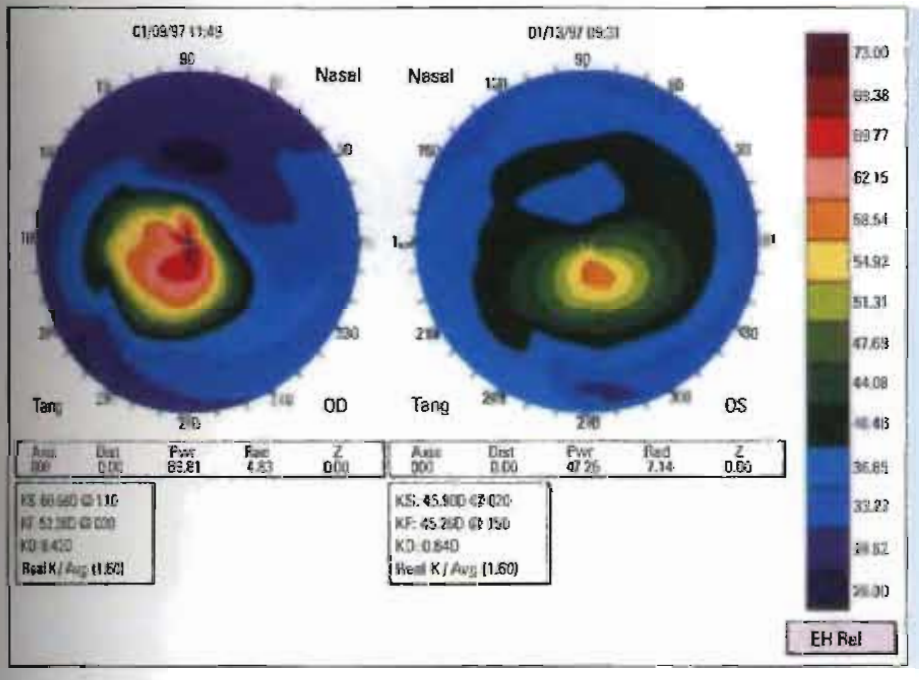

Fig. 5.123
Relative scale corneal maps showing advanced keratoconus in the right eye and an early paracentral cone in the left eye
(Courtesy of E. Morris)

Fig. 5.125
Apical corneal scarring in advanced keratoconus

Fig. 5.126
Acute hydrops in keratoconus

Fig. 5.127
Corneal scarring in keratoconus

2. **Rigid contact lenses** are required for higher degrees of astigmatism and provide a regular refracting surface. Advances in both lens design and material have increased the proportion of keratoconus patients who can use contact lenses. The following types of contact lenses can be used:
   - Standard, large diameter (9.7 mm), gas-permeable lenses in early cases.
   - Aspherical lenses for moderate nipple cones.
   - Small steep lenses for moderate to severe nipple cones.
   - Specially designed lenses for steep oval and globus cones when standard spherical lenses have failed.
   - Gas-permeable scleral lenses can be tried in extremely distorted corneas or very sensitive eyes which cannot tolerate corneal diameter contact lenses.
3. **Epikeratoplasty** is effective in patients intolerant to contact lenses without significant central corneal scarring.
4. **Keratoplasty**, penetrating or deep lamellar, is indicated in patients with advanced progressive disease, especially with significant corneal scarring (Fig. 5.127). Although clear grafts are obtained in over 85% of cases, optical outcomes may be compromised by residual astigmatism and anisometropia, necessitating contact lens correction for best acuity.

Pellucid marginal degeneration

Pellucid marginal degeneration is a rare condition which may be initially misdiagnosed as keratoconus, although occasionally the two may coexist and some patients may have atopy. Advanced cases with marked protrusion may be difficult to differentiate from keratoconus.

1. **Presentation** is in the third to fifth decades with increasing astigmatism
2. **Signs**
   - Bilateral, slowly progressive, crescent-shaped band of inferior corneal thinning extending from 4 to 8 o'clock (Fig. 5.128).

Fig. 5.128
Pellucid marginal degeneration (Courtesy of R. Visser)

- The area of thinning usually measures 1–2 mm in width and is separated from the limbus by normal cornea.
- The central cornea protrudes above the area of thinning, flattening in the vertical meridian with severe irregular against-the-rule astigmatism.
- Unlike keratoconus Fleischer rings and Vogt striae do not occur, but epithelial oedema may develop in the inferior cornea in advanced cases.

3. **Management**
   - *a. Spectacles* usually fail very early as irregular astigmatism increases.
   - *b. Gas-permeable* scleral lenses are often the best option.
   - *c. Surgical options*, none of which are ideal, in patients intolerant to contact lenses include wedge resection of diseased tissue, large penetrating keratoplasty, crescentic lamellar keratoplasty and thermokeratoplasty.

Keratoglobus

Keratoglobus is an extremely rare condition in which the entire cornea is abnormally thin. Possibly related to keratoconus, it may be associated with Leber congenital amaurosis and blue sclerae.

1. **Onset** is at birth.
2. **Signs**
   - In contrast with keratoconus the cornea develops globular, rather than conical ectasia.
   - Corneal thinning is generalized rather than at the apex of the protrusion (Fig. 5.129).
   - Acute hydrops occurs less commonly than in either keratoconus or pellucid marginal degeneration but the cornea is more prone to rupture on relatively mild trauma.
3. **Management** is with scleral contact lenses because the results of surgery are very poor.

Fig. 5.129
Keratoglobus

Neurokeratopathies

Neuroparalytic (exposure) keratopathy

This is the result of improper wetting of the ocular surface by the tear film because of inability to close the eyes on blinking (lagophthalmos), despite normal tear production.

1. **Causes** include facial nerve palsy, severe proptosis and scarring of the eyelids. The patient with a weak Bell phenomenon is at particular risk. Occasionally, corneal exposure during sleep may occur in normal individuals.
2. **Signs** range from mild inferior punctate epithelial changes (Fig. 5.130) to severe ulceration (Fig. 5.131).
3. **Treatment** if recovery is anticipated, involves frequent instillation of lubricants during the day and ointment and taping shut of the eyelids at night. If permanent, lid surgery is usually required (*see* Chapter 1).

Fig. 5.130
Inferior epithelial changes in neuroparalytic keratopathy

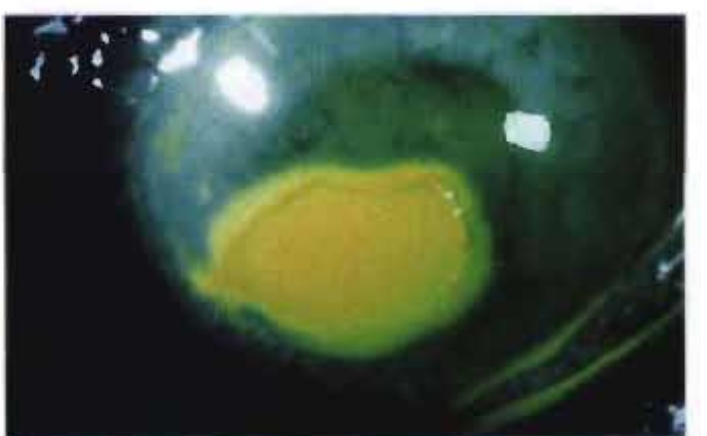

Fig. 5.131
Corneal ulcer in neuroparalytic keratopathy stained with fluorescein

Neurotrophic keratopathy

This occurs in an anaesthetic cornea. Although the pathogenesis is unclear, it appears that sensory innervation is vital to the health of the corneal epithelium. The loss of neural influences causes intracellular oedema, exfoliation of the epithelial cells and impairment of epithelial healing, culminating in persistent and progressive ulceration.

1. **Causes**
   - *a. Acquired* causes include section of the fifth nerve, herpes simplex and zoster keratitis, diabetes, leprosy, acoustic neuroma and abuse of topical anaesthetics.
   - *b. Congenital* causes include familial dysautonomia (Riley–Day syndrome), anhidrotic ectodermal dysplasia and congenital insensitivity to pain.
2. **Signs** tend to wax and wane, some patients developing serious lesions early and others after many years. In order of severity the corneal changes are as follows:
   - Grey, slightly opaque and oedematous epithelium (Fig. 5.132).
   - Punctate epithelial erosions most marked in the interpalpebral area.
   - Slow-healing epithelial defects which may become infected.
   - Stromal corneal melting and perforation are uncommon (Fig. 5.133).
3. **Prevention** involves the induction of protective ptosis by injection of botulinum toxin into the levator muscle, 3 days before any neurosurgical procedure on the trigeminal nerve to allow time for full effect. If toxin is not available, tarsorrhaphy should be performed.
4. **Treatment** of established keratopathy is aimed at promoting re-epithelialization with lubricants and patching. Other recently described treatment modalities include topical nerve growth factor drops and amniotic membrane transplantation.

Fig. 5.132
Epithelial changes in mild neurotrophic keratopathy

Fig. 5.133
Corneal perforation in neurotrophic keratopathy

Recurrent corneal erosion syndrome

The recurrent corneal erosion syndrome is a distressing condition characterized by disturbance of the epithelial basement membrane resulting in defective adhesion and recurrent breakdown of the epithelium. The condition most commonly follows superficial corneal trauma, especially a scratch. It may also occur in certain corneal dystrophies, particularly epithelial basement membrane dystrophy, as already described. Recurrent corneal erosions tend to be particularly troublesome in diabetic patients.

Clinical features

1. **Presentation** is typically on waking with sudden pain, lacrimation, photophobia and blurred vision, which usually resolve spontaneously within a few hours. Some patients experience several recurrences until normal attachment of the basal layer of the epithelium is restored.

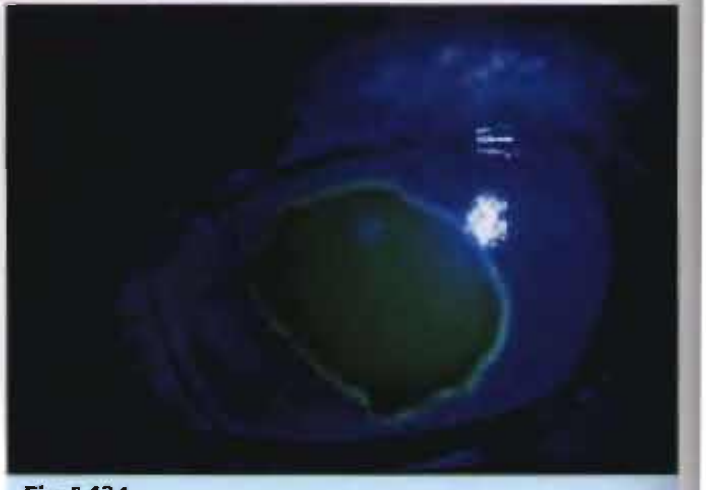

Fig. 5.134
Traumatic corneal macroerosion stained with fluorescein

2. **Signs**
   a. *Microerosions* are spontaneous small epithelial defects, associated with epithelial basement membrane dystrophy, which cause relatively mild symptoms.
   b. *Macroerosions* are extremely painful large epithelial defects with surrounding loosely adherent epithelium, most commonly associated with previous trauma (Fig. 5.134). Abrasions caused by a fingernail are particularly likely to progress to recurrent erosions.

NB: It is important to examine the fellow eye for evidence of corneal dystrophy.

Treatment of acute erosions

1. **Topical** treatment is with lubricants while the epithelium is healing. A mild cycloplegic (e.g. cyclopentolate) and a non-steroidal anti-inflammatory agent (e.g. ketorolac tromethamol 0.5%) may increase patient comfort.

NB: Although pressure patching has been standard treatment in the past it has become apparent that the cornea heals faster and the patient has less pain when it is not applied.

2. **Debridement** is indicated in severe cases with extensive devitalization and disadhesion of the epithelium. It is performed as follows:
   a. The zone of defective adhesion is determined by anaesthetizing the cornea and then touching the involved area with a sterile moistened cotton-tipped bud.
   b. Abnormal epithelium will become loose with minimal pressure and take on a grey colour.
   c. Debridement is then accomplished by first gently scrubbing the loose epithelium with a cellulose sponge and then removing it with small forceps.
   d. Instillation of cyclopentolate 1% and antibiotic ointment.

Prophylactic treatment

This should be considered in patients with frequent or severe recurrences.

1. **Topical lubricants** four times daily and at night for 8 weeks is usually effective for relatively mild cases.
2. **Extended-wear bandage contact lenses** with a low water content are useful if lubrication is ineffective. Lens wear has to be continued for 2 months until epithelial re-adhesion has occurred.
3. **Epithelial keratectomy** may be necessary for severe recalcitrant cases, particularly when associated with aberrant basement membrane in corneal dystrophies and degenerations. The procedure can be performed with an excimer laser (phototherapeutic keratectomy) or a Bard–Parker knife and involves removal of the entire epithelium which takes 5–7 days to regrow.
4. **Anterior stromal micropuncture** is an alternative treatment for recalcitrant post-traumatic erosions, for focal and peripheral lesions. It is performed at the slit-lamp and involves making multiple anterior stromal micropunctures with a bent 25-gauge needle. This incites focal microcicatrization with more secure epithelial adhesion. Treatment to the visual axis should be avoided if possible.
5. **Systemic tetracycline** 250 mg b.d. for 12 weeks may also be helpful. The mechanism of action is not fully understood and is probably not related to its antibacterial properties.

Drug-induced keratopathies

Chrysiasis

Chrysiasis is the deposition of gold in living tissue, occurring after prolonged administration of gold, usually in the treatment of rheumatoid arthritis. Virtually all patients on continuous chrysotherapy who have received a total dose of gold compound exceeding 1000 mg develop corneal deposits. Corneal chrysiasis is characterized by dust-like or glittering purple granules throughout the corneal stroma, more concentrated in the deep layers and the periphery. These findings are innocuous and therefore not an indication for cessation of therapy. Visually inconsequential lens deposits also develop in about 50% of patients treated for 3 or more years.

Vortex keratopathy

Vortex keratopathy (cornea verticillata) is characterized by whorl-like corneal epithelial deposits.

1. **Signs** (in chronological order)
   - Bilateral, fine greyish or golden-brown opacities in the inferior corneal epithelium.
   - Arborizing horizontal lines in a pattern resembling cat's whiskers, similar to the more common Hudson–Stähli line.

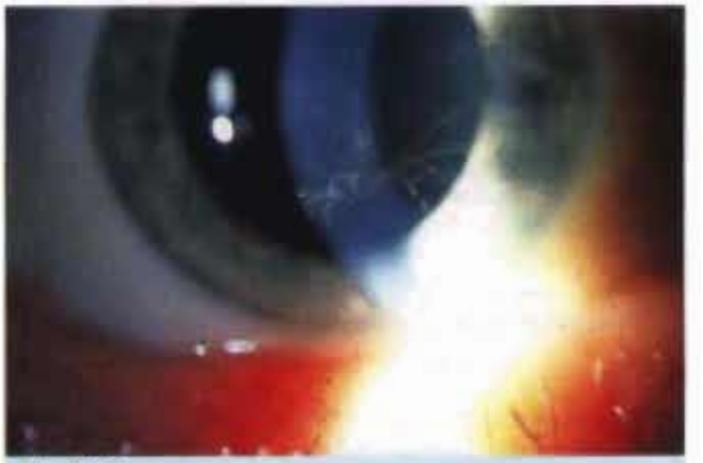

Fig. 5.135
Vortex keratopathy

- A whorl-like pattern which originates from a point below the pupil and swirls outwards, sparing the limbus (Fig. 5.135).

NB: Although deposits may involve the visual axis, vision is not impaired but some patients may experience haloes around lights.

2. Causes

a. Antimalarials (chloroquine and hydroxychloroquine) are common causes. Unlike retinopathy, keratopathy bears no relationship to dosage or duration of treatment. The changes are usually reversible on cessation of therapy, although they may clear despite continued administration.

b. Amiodarone is a drug used to treat cardiac arrhythmias. Virtually all patients on amiodarone develop keratopathy, which is reversible on discontinuation of medication. In general the higher the dose and the longer the duration of administration, the more advanced the corneal deposits. Visually inconsequential anterior subcapsular lens deposits also develop in about 50% of patients on moderate to high doses. Optic neuropathy is a rare complication.

NB: Vortex keratopathy also occurs in Fabry disease, which is a glycolipidosis caused by deficiency of the enzyme alpha-galactosidase A. Systemic features include angiokeratomas, cardiovascular and renal disease. Spoke-like lens opacities may also be present.

Metabolic keratopathies

Cystinosis

Cystinosis is a rare, AR, metabolic disorder characterized by widespread tissue deposition of non-protein cystine crystals as a result of a defect in lysosomal transport.

1. **Systemic features** include severe growth retardation, renal failure, hepatosplenomegaly and hypothyroidism. Patients with the most severe nephropathic form usually succumb before the second decade.
2. **Ocular features** are characterized by progressive deposition of cystine crystals in the conjunctiva and cornea which cause intense photophobia, blepharospasm, epithelial erosions and visual disability. Peripherally, crystals involve the entire stromal thickness, whereas centrally only the anterior two-thirds are affected (Fig. 5.136). Later, involvement of the iris, lens capsule and retina further affects vision.
3. **Treatment** involves topical 0.2% cysteamine for several weeks.

Immunoprotein deposits

Diffuse or focal immunoprotein deposition is a relatively uncommon manifestation of several systemic diseases,

Fig. 5.136
Corneal crystals in cystinosis

Fig. 5.137
Corneal crystals in monoclonal gammopathy

including multiple myeloma, Waldenström macroglobulinaemia, monoclonal gammopathy of unknown cause, certain lymphoproliferative disorders and leukaemia. Corneal involvement may be the earliest manifestation of the disease.

1. **Signs.** Gradual bilateral development of a band of multiple, punctate, flake-like opacities mostly at the level of the posterior stroma (Fig. 5.137).
2. **Treatment** should address the underlying systemic disease with cytotoxic chemotherapy or steroids. Severe corneal involvement may require penetrating keratoplasty.

Mucopolysaccharidoses

The mucopolysaccharidoses (MPS) are a group of inherited deficiencies of catabolic glycosidases necessary for hydrolysis of mucopolysaccharides. The altered metabolite accumulates in intracellular vacuoles in various tissues and organs and is also detectable in the urine.

Fig. 5.138
Facial coarseness in Hurler syndrome

Fig. 5.139
Corneal clouding in Hurler syndrome

1. **Inheritance** is AR with the exception of the two subtypes of Hunter disease which are X-linked recessive.
2. **Systemic features**, which vary with the type of MPS, include facial coarseness (Fig. 5.138), skeletal anomalies, mental retardation and heart disease.
3. **Corneal deposits** are generally associated with skeletal anomalies and occur in all MPS except Hunter and Sanfilippo. In Hurler and Scheie they are most severe (Fig. 5.139) and present at birth. Corneal clouding in this setting should be differentiated from that secondary to congenital glaucoma, rubella keratopathy, congenital hereditary endothelial dystrophy and birth trauma.
4. **Other ocular features**
   a. *Pigmentary retinopathy* occurs in all except Morquio and Maroteaux–Lamy.
   b. *Optic atrophy* occurs in all six MPS and is most severe in Hurler.
   c. *Glaucoma* is rare.

Wilson disease

Wilson disease (hepatolenticular degeneration) is a rare condition caused by a deficiency of caeruloplasmin. It is characterized by a widespread deposition of copper in the tissues.

1. **Presentation** is with liver disease, basal ganglia dysfunction or psychiatric disturbances.
2. **Corneal deposits** of copper are present in nearly all patients. The classic Kayser–Fleischer ring, located at the peripheral part of Descemet membrane, appears as a zone of granules which change colour under different types of illumination (Fig. 5.140). The copper is deposited preferentially in the vertical meridian and may disappear with penicillamine therapy.

> *NB:* An early Kayser–Fleischer ring is best detected on gonioscopy.

3. **Anterior capsular green 'sunflower' cataract** is seen in some patients.

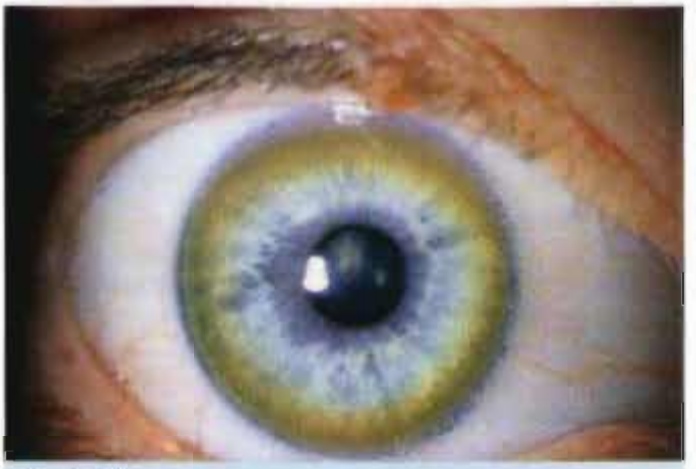

Fig. 5.140
Kayser–Fleischer ring in Wilson disease (Courtesy of R. Chopdar)

Congenital corneal anomalies

Microcornea

This is a rare unilateral or bilateral condition. Inheritance is usually AD.

1. **Signs**. The adult horizontal corneal diameter is 10 mm or less, the anterior chamber is shallow but other dimensions normal (Fig. 5.141).

Fig. 5.141
Microcornea (Courtesy of J. Salmon)

Fig. 5.142
Megalocornea

2. **Ocular associations** include glaucoma (initially closed and later open angle), congenital cataract, cornea plana, leukoma, iris abnormalities, microphakia, optic nerve hypoplasia and hypermetropia.
3. **Systemic associations** include fetal alcohol, Turner, Ehlers–Danlos, Weill–Marchesani, Waardenburg, Nance–Horan and Cornelia de Lange syndromes.

Megalocornea

This is a rare, bilateral, non-progressive enlargement of the cornea affecting males which must not be confused with buphthalmos due to congenital glaucoma. Inheritance is X-linked recessive.

1. **Signs**. Corneal diameter 13 mm or more, very deep anterior chamber, high myopia and astigmatism but normal visual acuity (Fig. 5.142). Lens subluxation may occur due to zonular stretching.
2. **Systemic associations** include Marfan, Apert, Ehlers–Danlos and Down syndromes, osteogenesis imperfecta, progressive facial hemiatrophy, renal carcinoma and mental handicap.

Cornea plana

This is a rare bilateral condition.

1. **Signs**. Severe decrease of corneal curvature (K readings 20–30 D), hypermetropia, shallow anterior chamber and a predisposition to angle closure glaucoma (Fig. 5.143).
2. **Ocular** associations include microcornea, sclerocornea, microphthalmos and Peters anomaly.

Posterior keratoconus

This is an uncommon, unilateral, non-progressive increased curvature of the posterior corneal surface. The anterior corneal surface is normal. Due to similar refractive indices of cornea and aqueous humour vision is minimally affected unless corneal clouding is present. Posterior keratoconus is divided into two types:

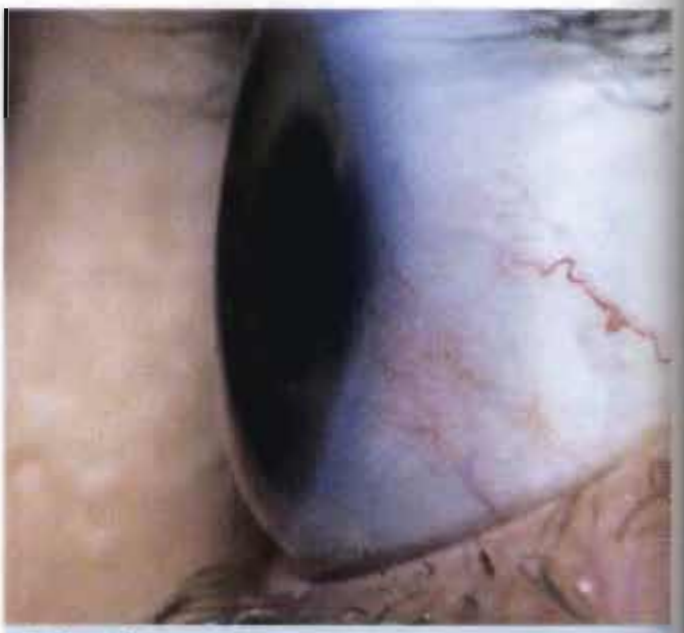

Fig. 5.143
Cornea plana (Courtesy of R. Visser)

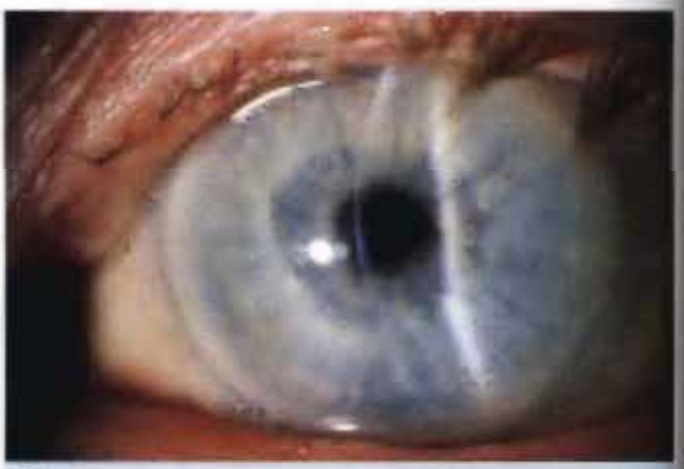

Fig. 5.144
Posterior keratoconus (Courtesy of S. Johns)

1. **Generalis**, in which there is an increase in curvature of the entire posterior corneal surface.
2. **Conscriptus**, in which there is a localized paracentral or central posterior corneal indentation (Fig. 5.144).

Sclerocornea

This is a rare, usually bilateral condition characterized by opacification and vascularization of the peripheral or entire cornea. If restricted to peripheral cornea the resulting 'scleralization' makes the cornea appear smaller (Fig. 5.145).

Keratectasia

This is a very rare, usually unilateral condition characterized by severe corneal opacification and protuberance between the eyelids. It is thought to be the result of intrauterine keratitis and perforation (Fig. 5.146).

Fig. 5.145
Sclerotornea (Courtesy of J. Salmon)

Fig. 5.146
Keratectasia

Contact lenses

Therapeutic uses

The risks of fitting a lens to an already compromised eye is greater than with lens wear for cosmetic reasons. The balance between benefit and risk should therefore be carefully considered. Close monitoring is vital to ensure early diagnosis and treatment of complications such as microbial keratitis. The choice of lens type is dictated by the nature of the ocular pathology.

Optical

To improve visual acuity when this cannot be achieved by spectacles in the following conditions:

1. **Irregular astigmatism** associated with keratoconus can be corrected with a rigid contact lens long after spectacles have failed and long before corneal grafting becomes necessary. Patients with astigmatism following corneal grafting may also benefit.
2. **Superficial corneal irregularities** can be neutralized by a rigid contact lens, which provides a smoother and optically more regular surface. Visual acuity can thus be improved, provided the irregularities are not too severe.
3. **Anisometropia** in which binocular vision cannot be achieved by spectacles (due to aniseikonia and prismatic effects) as may occur following cataract surgery.

Promotion of epithelial healing

1. **Persistent epithelial defects** often heal more quickly if the regenerating corneal epithelium is protected from the constant rubbing action of the lids. This allows the development of hemidesmosomal attachments to the basement membrane.
2. **Recurrent corneal erosions**, if associated with epithelial basement membrane dystrophy, may require long-term lens wear. In post-traumatic cases, lens wear can usually be discontinued after a few weeks. Lens wear may also provide comfort.

Pain relief

1. **Bullous keratopathy** can be managed with soft bandage contact lenses, which relieve pain by protecting the exposed corneal nerve endings from the shearing force of the eyelid during blinking. The lens may also flatten bullae into diffuse fine epithelial oedema. Instillation of hypertonic 5% saline may further osmotically reduce oedema and improve vision. The bullae gradually subside as corneal scarring supervenes and the patient can be weaned off lens wear.
2. **Wet filamentary keratitis** associated with profuse lacrimation, as seen in patients with brain stem strokes

and essential blepharospasm, can be treated with soft contact lenses and preservative-free acetylcysteine.
3. **Protection of corneal epithelium** from aberrant lashes.
4. **Thygeson superficial punctate keratitis.**

Preservation of corneal integrity

1. **A descemetocele** can be temporarily capped with a tight-fitting large-diameter soft or scleral lens to prevent perforation and allow natural healing to occur.
2. **Splinting** and apposition of the edges of a small corneal wound can be achieved by a contact lens which supports the cornea during healing. Examples include trauma, graft dehiscence, wound gape following cataract surgery, leaking trabeculectomy and accidental perforation during radial keratotomy. Slightly larger perforations may be sealed with glue (cyanoacrylate adhesive) followed by insertion of a bandage contact lens to protect the glue and prevent irritation of the lids from the glue's rough surface (Fig. 5.147).

Miscellaneous

1. **Ptosis props** to support the upper lids in patients with ocular myopathies.
2. **Maintenance of the fornices** to prevent symblepharon formation in eyes with cicatrizing conjunctivitis.
3. **Drug delivery** can be enhanced by a hydrogel lens imbibed with topical medication which increases exposure to the drug.

Complications

Allergic conjunctivitis

1. **Cause** is allergy to thiomersal, a preservative in contact lens care solutions, which was formerly a common problem with soft contact lenses. At one time, at least 10% of soft contact lens wearers were allergic to thiomersal. Fewer solutions now contain this ingredient.

Fig. 5.147
Bandage contact lens following the application of glue to seal a corneal perforation

Fig. 5.148
Fine papillary reaction in contact lens-induced allergic conjunctivitis

2. **Presentation** is with redness, burning and itching soon after lens insertion. These symptoms may develop within days to months following initial exposure to thiomersal.
3. **Signs**
   - Perilimbal injection and a fine papillary conjunctival reaction (Fig. 5.148).
   - Grey epithelium extending from the superior limbus towards the axial cornea.
4. **Treatment** involves avoidance of thiomersal. The lenses should be disinfected with heat and non-preserved saline or with a 3% hydrogen peroxide system.

Giant papillary conjunctivitis (GPC)

1. **Causes**
   - Irritation of the superior palpebral conjunctiva by the edge of a poorly fitting contact lens.
   - Allergy to lens material. Although any contact lens can cause GPC, soft lenses are most frequently implicated.
   - An immunological reaction to the contact lens deposits, especially proteins (Fig. 5.149).

Fig. 5.149
Contact lens deposits (Courtesy of C. Barry)

NB: GPC may also occur secondary to protruding corneal sutures (see Fig. 6.5) and poorly fitting ocular prostheses.

2. **Presentation** may be months or years after beginning lens wear, with ocular itching after lens removal, increased mucus production in the morning, photophobia and decreased lens tolerance. Blurred vision may also occur either from deposits on the lens or when the lens is pulled towards the upper fornix by the upper lid.
3. **Signs**
   - The spectrum of changes on the upper tarsal conjunctiva ranges from a mild papillary response to the full-blown picture of GPC characterized by giant papillae (>0.3 mm) (Fig. 5.150).
   - Excessive mucus in the eye and on the contact lens.
   - Trantas' dots, limbitis and peripheral corneal infiltration may be present.
   - Mechanical ptosis in severe cases.

Fig. 5.150
Contact lens-induced giant papillary conjunctivitis (Courtesy of C Barry)

4. **Treatment**
   - Lens hygiene should be optimized and the patient reinstructed in the use of care solutions.
   - Lens fitting may require adjustment to decrease edge lift and regular replacement to minimize protein deposition.
   - Change in lens type from soft to gas-permeable may be beneficial because the latter are less likely to cause GPC.
   - Topical treatment with a mast cell stabilizer is often effective but long-term steroids should be avoided.

Corneal complications

1. **Epithelial oedema** due to hypoxia secondary to overwear is usually reversible.
2. **Corneal vascularization**, most often at the superior limbus, may develop in response to lens-induced hypoxia, especially with extended-wear lenses. New vessels are typically subepithelial, although deeper stromal vascularization may also occur.
3. **Sterile corneal infiltrates** are usually peripheral and may be epithelial, subepithelial or anterior stromal. Usually asymptomatic and detected during routine follow-up, they usually disappear once contact lens wear has been discontinued. Resumption of lens wear is usually possible after revision of lens care and improvement of lens fit. A short course of topical steroids may also speed up resolution. It is, however, extremely important to remember that a corneal infiltrate may be an early manifestation of microbial keratitis. Epithelial integrity is of diagnostic importance. If breached it implies infection. If intact the infiltrate is probably sterile. Pain, discharge and anterior uveitis are also signs of infection.
4. **Microbial keratitis** is the most serious complication.
5. **Corneal warping** resulting in severe and permanent astigmatism may occur in some eyes as a response to chronic hypoxia, for example, following prolonged wear of impermeable lenses.

CHAPTER 6

Corneal and Refractive Surgery

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Keratoplasty

Keratoplasty (corneal transplantation, grafting) is an operation in which abnormal corneal host tissue is replaced by healthy donor cornea. A corneal graft may be (a) *full-thickness (penetrating)* or (b) *partial-thickness (lamellar or deep lamellar)*.

Penetrating keratoplasty

Indications

1. **Optical** keratoplasty is most often performed to improve vision. Important indications include pseudophakic bullous keratopathy, keratoconus, dystrophies, degenerations and scarring.
2. **Tectonic** grafting may be carried out to restore or preserve corneal integrity in eyes with severe structural changes such as stromal thinning and descemetoceles.
3. **Therapeutic** transplantation may afford removal of infected corneal tissue in eyes unresponsive to antimicrobial therapy.
4. **Cosmetic** grafting may rarely be performed to improve the appearance of the eye.

Donor tissue

Donor tissue should be removed within 24 hours of death. Corneas from infants are usually not used, being floppy and likely to result in high astigmatism. Corneas from donors over the age of 70 years may also be inappropriate due to low endothelial cell counts. Preoperative evaluation of donor tissue includes slit-lamp examination and, ideally, specular microscopy. Corneas should not be utilized under the following circumstances:

- Death of unknown cause.
- Infectious diseases of the CNS (e.g. Creutzfeldt–Jakob disease, systemic sclerosing panencephalitis, progressive multifocal leucoencephalopathy).
- Certain systemic infections (e.g. AIDS, viral hepatitis, syphilis, septicaemia).
- Leukaemia and disseminated lymphoma.
- Intrinsic eye disease (e.g. malignancy, active inflammation) or previous intraocular surgery.

Prognostic factors

The following factors may adversely affect the prognosis of a corneal graft and should therefore be addressed prior to surgery:

- Abnormalities of the eyelids such as blepharitis, trichiasis, ectropion and entropion. They should be corrected before surgery.
- Tear film dysfunction.
- Recurrent or progressive forms of conjunctival inflammation, such as atopic conjunctivitis and ocular cicatricial pemphigoid.
- Severe stromal vascularization, absence of corneal sensation, extreme thinning at the proposed host–graft junction and active corneal inflammation.
- Anterior synechiae.
- Uncontrolled glaucoma.
- Uveitis.

> ***NB:*** In general, the most favourable cases are localized scars, keratoconus and dystrophies.

Surgical technique

1. **Determination of graft size** is done preoperatively with a variable slit beam and operatively by trial placement of trephines with different diameters. Grafts of diameter 8.5 mm or more are prone to postoperative anterior synechiae formation, vascularization and increased intraocular pressure. An ideal size is 7.5 mm; grafts smaller than this may give rise to high astigmatism.
2. **Excision of donor cornea** should always precede that of host cornea. Donor tissue is prepared by trephining a previously excised corneoscleral button, endothelial side up in a concave Teflon block. Alternatively, the donor may be trephined from the intact donor globe having first injected air or viscoelastic substance into the anterior chamber. The donor button is usually about 0.25 mm larger in diameter than the planned diameter of the host opening, to facilitate watertight closure, minimize postoperative flattening and reduce the possibility of postoperative glaucoma.
3. **Excision of diseased host tissue** is then carried out taking care not to damage the iris and lens with the trephine.

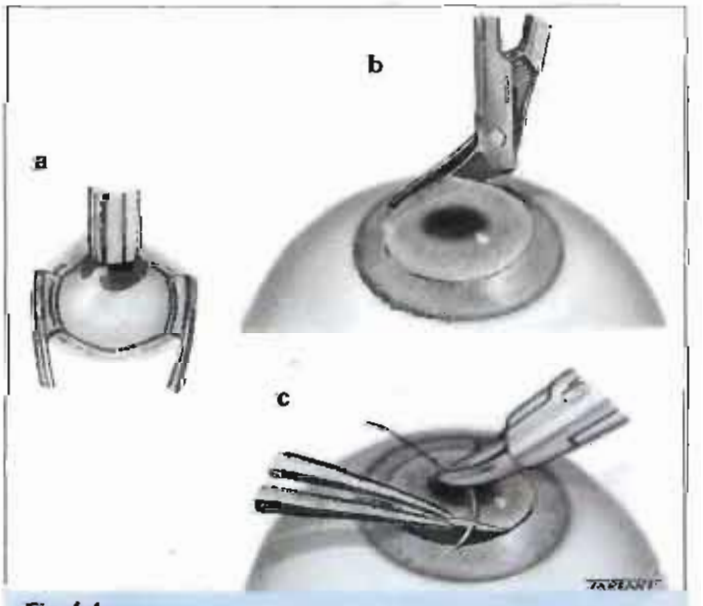

Fig. 6.1
Technique of penetrating keratoplasty. (a) Trephination of host cornea; (b) completion with scissors; (c) suturing of donor button

a. The lens can be protected to some extent by achieving preoperative miosis with topical pilocarpine and employment of a viscoelastic substance during surgery.
b. Recipient cornea may be excised with a manual (Fig. 6.1a), motorized or vacuum trephine. The latter adheres to recipient cornea and reduces slippage. Rapid decompression of the eye, with its attendant risks of prolapse of intraocular contents and expulsive suprachoroidal haemorrhage, can be avoided by performing a partial-thickness trephination and then entering the anterior chamber with a diamond knife.
c. Excision can then be completed with knife or scissors (Fig. 6.1b).

4. **Fixation of donor tissue** is usually with 10-0 monofilament nylon. The corneal 'bites' are almost full-thickness (Fig. 6.1c) to ensure that Descemet membrane is apposed and posterior wound gape avoided.
   a. Four interrupted cardinal sutures are initially placed.
   b. Closure is then completed with interrupted sutures (Fig. 6.2), continuous running sutures (Fig. 6.3), or a combination of both.
5. **Replacement** of viscoelastic substance with balanced salt solution.

Postoperative management

1. **Topical**
   a. Steroids are used to reduce the risk of immunological graft rejection. After initial administration q.i.d. for a few weeks, the dose may be tapered, depending on the condition of the eye. Steroids are, however, usually continued at low doses such as once daily for a year or more.

> *NB:* Unpreserved drops should be used until the graft has epithelialized.

   b. Mydriatics b.d. for 2 weeks, or longer if uveitis persists.
2. **Oral** aciclovir, may be used in the context of pre-existing herpes simplex keratitis to minimize the risk of recurrence.
3. **Removal of sutures** when the graft–host junction has healed. This is usually after 9–12 months, although in elderly patients it may take much longer.

Fig. 6.3
Continuous suture

Fig. 6.4
Protruding suture

Fig. 6.2
Interrupted sutures

Fig. 6.5
Papillary hypertrophy due to irritation by a protruding suture

4. **Rigid contact lenses** may be required to optimize visual acuity in eyes with astigmatism but not until all sutures have been removed.

Postoperative complications

1. **Early** complications include persistent epithelial defects, irritation by protruding sutures (Fig. 6.4) which may give rise to papillary hypertrophy (Fig. 6.5), wound leak, flat anterior chamber, iris prolapse, uveitis, elevated intraocular pressure and infection.
2. **Late** complications include astigmatism, recurrence of initial disease process on the graft, late wound separation, retrocorneal membrane formation, glaucoma and cystoid macular oedema.

Graft failure

1. **Early** failure is characterized by cloudiness of the graft from the first postoperative day (Fig. 6.6). It is caused by endothelial dysfunction resulting from defective donor endothelium or operative trauma.
2. **Late** failure is usually due to immunological graft rejection. About 50% of cases occur within the first 6 postoperative months, and the vast majority within 1 year. Rejection may affect either the epithelium or endothelium.
   a. ***Epithelial*** rejection is characterized by a linear epithelial opacity (Fig. 6.7) which may be relatively asymptomatic and of little long-term consequence. This is followed by the appearance of multiple small subepithelial infiltrates, reminiscent of adenoviral keratitis (Krachmer spots) (Fig. 6.8), which may be associated with mild iritis. Intensive topical steroids are usually effective in reversing this phenomenon.
   b. ***Endothelial*** rejection is very much more serious, since endothelial cells destroyed by the immunological attack cannot regenerate. Permanent corneal oedema may therefore result. Initially, endothelial rejection is characterized by iritis and inflammation at the graft–host junction (Fig. 6.9). This is followed by the

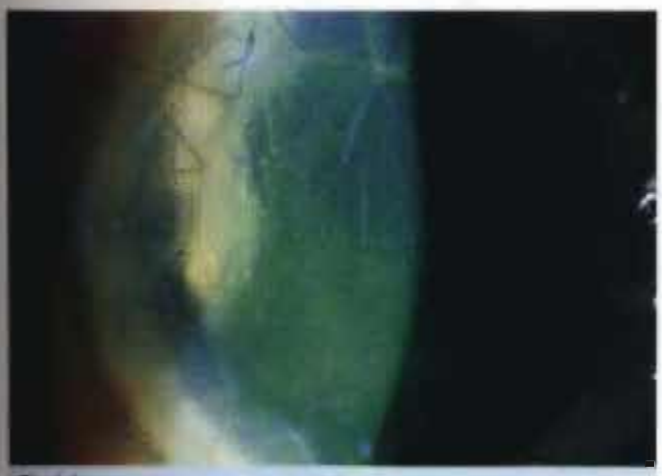

Fig. 6.6
Cloudy graft due to early endothelial failure

Fig. 6.8
Multiple small subepithelial infiltrates associated with late epithelial rejection (Courtesy of D. Easty)

Fig. 6.7
Linear epithelial opacity associated with late epithelial rejection (Courtesy of D. Easty)

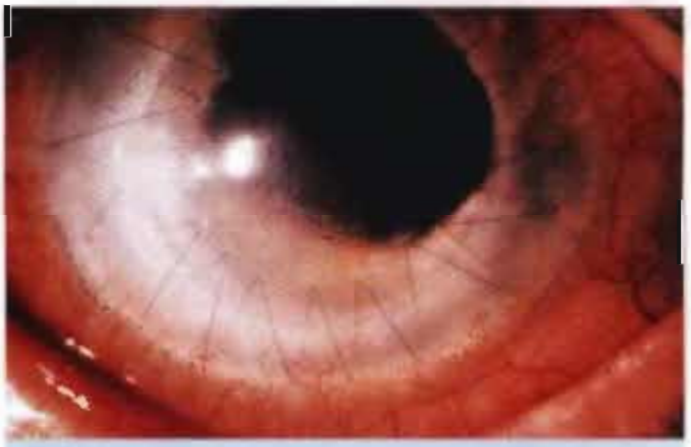

Fig. 6.9
Keratic precipitates and inflammation at the graft–host junction associated with early endothelial rejection (Courtesy of D. Easty)

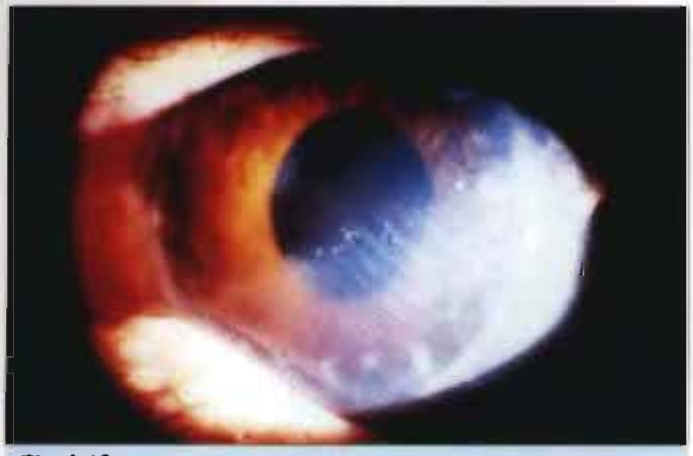

Fig. 6.10
Linear endothelial precipitates (Khodadoust line) and corneal oedema associated with severe endothelial rejection (Courtesy of D. Easty)

development of a linear arrangement of endothelial precipitates (Khodadoust line) and corneal oedema (Fig. 6.10). Treatment involves intensive topical and periocular steroids. Occasionally systemic immunosuppression may be necessary.

Lamellar keratoplasty

Lamellar keratoplasty involves partial-thickness excision of the corneal epithelium and stroma so that the endothelium and part of the deep stroma are left behind.

1. **Indications**
   - Opacification of the superficial one-third of the corneal stroma not caused by potentially recurrent disease.
   - Marginal corneal thinning or infiltration as in recurrent pterygium. Terrien marginal degeneration and limbal dermoids or other tumours.
   - Localized thinning or descemetocele formation.
2. **Technique**. This is similar to that of penetrating keratoplasty except that only a partial-thickness area of cornea is grafted.

Deep lamellar keratoplasty

Deep lamellar keratoplasty is a relatively new technique in which all opaque corneal tissue is removed almost to the level of Descemet membrane. The theoretical advantage is the decreased risk of rejection because the endothelium, a major target for rejection, is not transplanted.

1. **Indications**
   - Disease involving the anterior 95% of corneal thickness with a normal endothelium and absence of breaks or scars in Descemet membrane.
   - Chronic inflammatory disease such as atopic keratoconjunctivitis which carries an increased risk of graft rejection.
2. **Advantages**
   - No risk of endothelial rejection although epithelial rejection may occur.
   - Less astigmatism and a structurally stronger globe as compared with penetrating keratoplasty.
   - Increased availability of graft material since endothelial quality is irrelevant.
3. **Disadvantages**
   - Difficult and time-consuming technique with a high risk of perforation in older patients.
   - Interface haze may limit best final visual acuity.
4. **Surgical technique** (developed by R. Melles).
   a. A superior scleral pocket is created similar to that for phacoemulsification and the anterior chamber filled with air.
   b. A lamellar dissection is performed across almost the entire cornea (Fig. 6.11). A zone of total internal reflection in front of the dissector equal to twice the thickness of the underlying stroma is used to judge the depth of the dissection.
   c. The dissection space is expanded with viscoelastic substance (Fig. 6.12).
   d. The superficial corneal lamella is trephined and removed (Fig. 6.13).
   e. Viscoelastic substance is washed away and air released from the anterior chamber.
   f. After removal of the donor endothelium, a full-thickness graft is sutured in place (Fig. 6.14).

NB: The major difficulty lies in judging the depth of the corneal dissection as close as possible to Descemet membrane without perforating.

Fig. 6.11
Lamellar dissection in deep lamellar keratoplasty (Courtesy of C. Murphy and T. Wells)

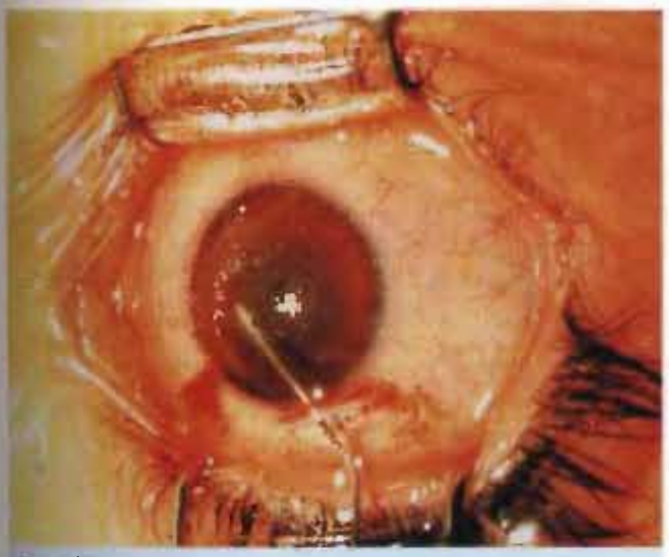

Fig. 6.12
Expansion of dissected space with viscoelastic substance in deep lamellar keratoplasty (Courtesy of C. Murphy and T. Wells)

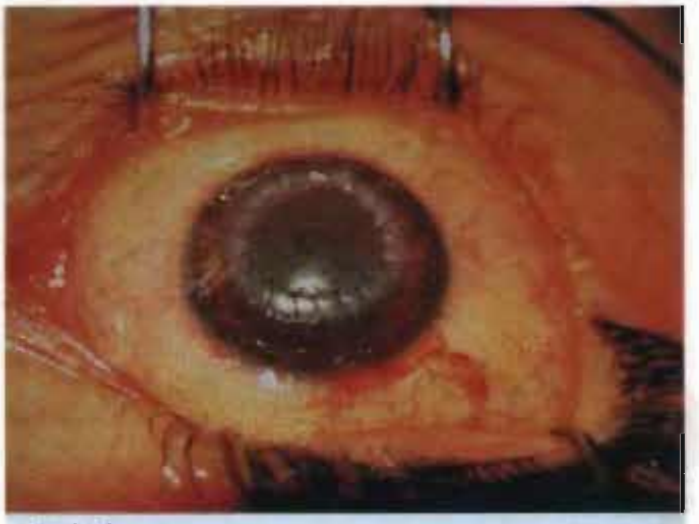

Fig. 6.14
Completed deep lamellar keratoplasty (Courtesy of C. Murphy and T. Wells)

Fig. 6.13
Removal of superficial lamella in deep lamellar keratoplasty (Courtesy of C. Murphy and T. Wells)

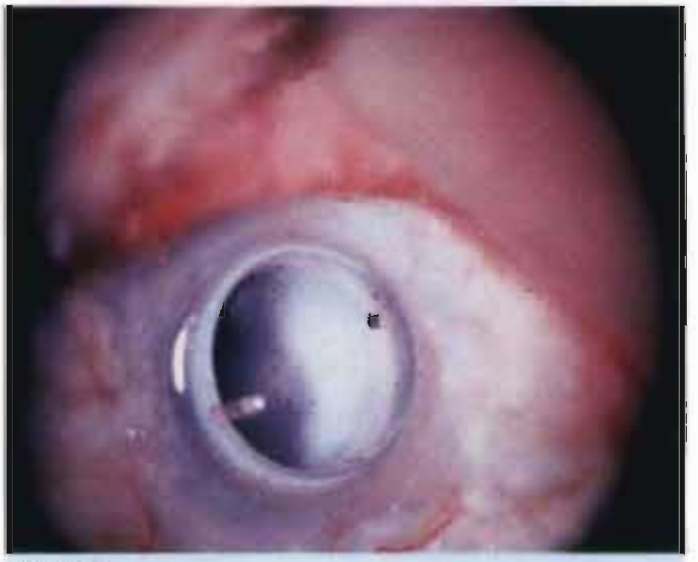

Fig. 6.15
Keratoprosthesis

5. **Postoperative management** is similar to penetrating keratoplasty except that less topical steroids are needed and sutures can be usually removed after 6 months.

Keratoprostheses

Keratoprostheses are artificial corneal implants (Fig. 6.15) used in patients unsuitable for keratoplasty. The modern osteo-odonto-keratoprosthesis consists of the patient's own tooth root and alveolar bone which supports the central optical cylinder. Surgery is difficult and time consuming and is performed in two stages 2–4 months apart.

1. Indications

- Patients with bilateral blindness with visual acuity of hand movements or less but normal optic nerve and retinal function (i.e. accurate light projection, good pupillary responses if obtainable, normal electrophysiological tests and absence of retinal detachment on ultrasonography).
- Severe, debilitating but inactive anterior segment disease with no realistic chance of success from conventional keratoplasty (e.g. Stevens–Johnson syndrome, ocular cicatricial pemphigoid, chemical burns or trachoma).
- Multiple previous failed corneal grafts.
- Normal intraocular pressure with or without medication.

- Absence of active ocular surface inflammation.
- Good patient motivation.

2. **Complications** include glaucoma, retroprosthesis membrane formation, tilting or extrusion of the cylinder and endophthalmitis.
3. **Results.** Approximately 80% of patients experience visual improvement which varies from CF to 6/12 or even better. Poor visual outcome is often associated with pre-existing optic nerve or retinal dysfunction.

Refractive surgery

Introduction

Refractive surgery encompasses a range of procedures aimed at changing the refraction of the eye by altering the cornea and/or crystalline lens, which constitute the principal refracting components. Refractive errors corrected by such procedures include myopia, hypermetropia and astigmatism. The surgical correction of presbyopia is still in its infancy and will not be described.

> ***NB:*** To settle any contact lens-induced corneal distortion, soft contact lenses should be discontinued 2 weeks before keratometry and hard lenses for 1 week for each year of wear.

Correction of myopia

1. **Corneal surgery** is aimed at flattening the cornea.
   a. ***Radial keratotomy*** involves making radial incisions in peripheral cornea (Fig. 6.16). The procedure works reasonably well for low degrees of myopia. However, since the advent of laser procedures its use has diminished.
   b. *Photorefractive keratectomy* (PRK — *see* later).
   c. ***Laser in-situ keratomileusis*** (LASIK — *see* later).
   d. ***Intrastromal plastic rings*** which cause central flattening can be used to correct low myopia but are at a very early stage of development. The procedure avoids the visual axis and is potentially reversible.
2. **Lens surgery**
   a. ***Clear lens extraction*** gives very good visual results but carries a small risk of retinal detachment.
   b. ***Phakic posterior chamber intraocular lens implantation*** (implantable contact lenses) may be used for high myopia. The lens is inserted behind the iris, in front of the crystalline lens and supported in the ciliary sulcus. The lens is composed of material derived from collagen with a power of −3 D to −20.50 D. Short-term visual results are promising; however, this procedure should be used with caution because it may be associated with uveitis, endothelial cell loss and cataract formation.
   c. ***Phakic anterior chamber intraocular lens implantation*** with angle support may also be used to correct high myopia. This appears to be well tolerated by the corneal endothelium; apart from pupillary distortion other short-term problems are uncommon.

Correction of hypermetropia

1. **Corneal surgery** aimed at steepening the central cornea is at a much earlier stage than that for myopia.
   a. *PRK* can correct low degrees of hypermetropia.
   b. *LASIK* can correct up to 4 D.
   c. ***Laser thermal keratoplasty*** with a holmium laser can correct low hypermetropia. Laser burns are placed in one or two rings in the corneal periphery (Fig. 6.17). The resultant thermally induced stromal shrinkage is accompanied by increase in central corneal curvature. This change decays over time but the procedure can be repeated.
2. **Lens surgery** involving phakic intraocular lens implantation is at an early stage.

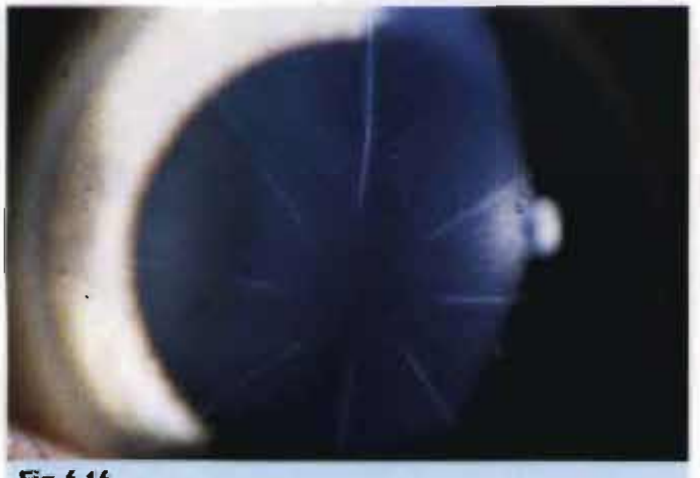

Fig. 6.16
Appearance following radial keratotomy

Fig. 6.17
Appearance following laser thermal keratoplasty (Courtesy of H. Nano Jr)

Correction of astigmatism

1. Corneal surgery

a. Arcuate keratotomy involves making paired arcuate incisions on opposite sides of the cornea in the axis of the correcting 'plus' cylinder (the steep meridian). The resultant flattening of the steep meridian coupled with a smaller steepening of the flat meridian at 90° to the incisions reduces astigmatism. The desired result can be controlled by varying the length, depth of the incisions and their distance from the optical centre of the cornea. Arcuate keratotomy may be combined with compression sutures placed in the perpendicular meridian, when treating large degrees of astigmatism such as may occur following penetrating keratoplasty.

b. PRK can correct up to 3 D.

c. LASIK can correct up to 5 D.

2. Lens surgery involves using a toric intraocular implant at the time of cataract extraction. However, postoperative rotation of the implant away from the desired axis may occur.

Photorefractive keratectomy

Photorefractive keratectomy (PRK) is performed with the excimer laser, which can accurately ablate corneal tissue to an exact depth with minimal disruption of surrounding tissue. Myopia is treated by ablating the central anterior corneal surface so that it becomes flatter (Fig. 6.18); approximately 10 μm of ablation corrects 1 D of myopia. Hypermetropia is treated by ablation of the periphery so that the centre becomes steeper. PRK is able to correct myopia up to 6 D, astigmatism up to 3 D and low hypermetropia. Since the advent of LASIK the procedure is being performed less frequently and is largely reserved for patients who are unsuitable for LASIK, such as those with very thin corneas.

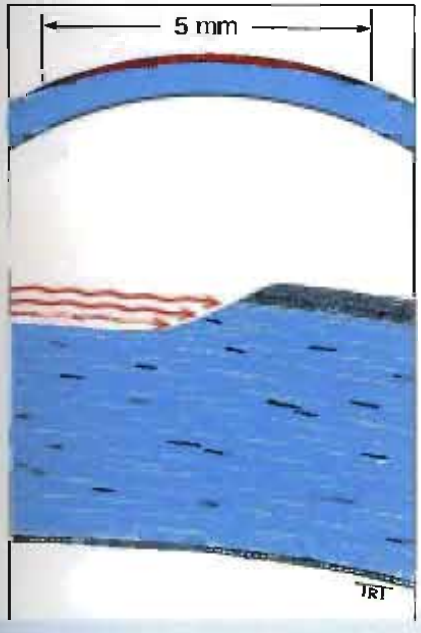

Fig. 6.18
Principles of photorefractive keratectomy for myopia

1. Technique

a. The visual axis is marked and the corneal epithelium removed.

b. The patient fixates on the aiming beam of the laser.

c. The laser is applied to ablate only Bowman layer and anterior stroma (Fig. 6.19). This usually takes 30–60 seconds.

The cornea usually heals within 48–72 hours. A subepithelial haze (Fig. 6.20) invariably develops within 2 weeks and persists for 1–6 months. It rarely causes diminished visual acuity but may produce night glare.

2. Complications include slow-healing epithelial defects, corneal haze and haloes, poor night vision and regression of refractive correction. Uncommon problems include decentred ablations, scarring, abnormal epithelial healing, irregular astigmatism, hypoaesthesia, sterile infiltrates, infection and acute corneal necrosis.

Fig. 6.19
Appearance during photorefractive keratectomy (Courtesy of C. Barry)

Fig. 6.20
Subepithelial corneal haze following photorefractive keratectomy (Courtesy of H. Nano Jr)

Laser in-situ keratomileusis

Laser in-situ keratomileusis (LASIK) is currently the most frequently performed refractive procedure. It is more versatile than PRK and can correct hypermetropia of up to 4 D, astigmatism of up to 5 D and myopia of up to 12 D depending on corneal thickness. To prevent corneal ectasia, a residual corneal base of 250 μm thickness must remain after the flap has been cut and tissue ablated. The amount of tissue removed and the total treatment is therefore limited by the original corneal thickness (on pachymetry). The thickness of the flap can be varied but thinner flaps are more difficult to handle and are more prone to wrinkling.

1. Technique

a. A suction ring is applied to the globe, which raises the intraocular pressure to over 65 mmHg. This may temporarily occlude the central retinal artery and extinguish vision.

b. The ring is centred on the cornea and provides a guide track into which an automated microkeratome is inserted.

c. The keratome is mechanically advanced across the cornea to create a very thin flap, which is reflected (Fig. 6.21).

d. Suction is released and the bed is treated with the excimer laser as for PRK.

e. The flap is repositioned and allowed to settle undisturbed for 30 seconds.

2. Complications

a. Operative flap-related complications involving the microkeratome include buttonholes, thin flaps, flap amputation, incomplete or irregular flaps, and rarely corneal perforation.

b. Postoperative

- Wrinkling (Fig. 6.22), distortion or dislocation of the flap.
- Epithelial defects may predispose to epithelial ingrowth under the flap.
- Diffuse lamellar keratitis is characterized by streaky white granular infiltrates confined to the flap interface ('shifting sands of the Sahara') which may resolve spontaneously within a few days or with the use of topical steroids if persistent.
- Other complications include peripheral corneal infiltrates, late infectious keratitis, anterior segment ischaemia and optic neuropathy presumably due to raised intraocular pressure.

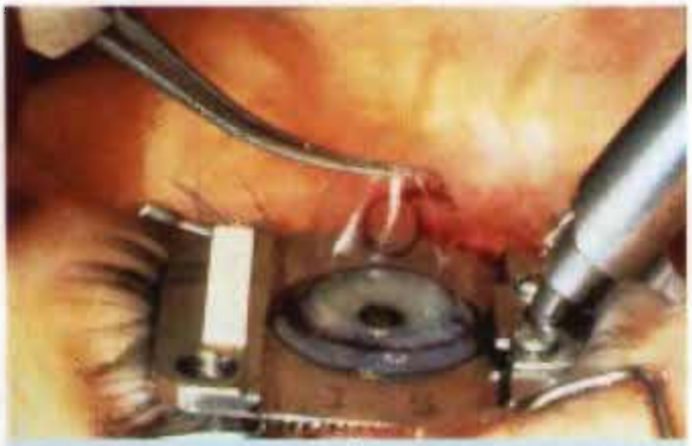

Fig. 6.21
Corneal flap created with a keratome during LASIK (Courtesy of Eye Academy)

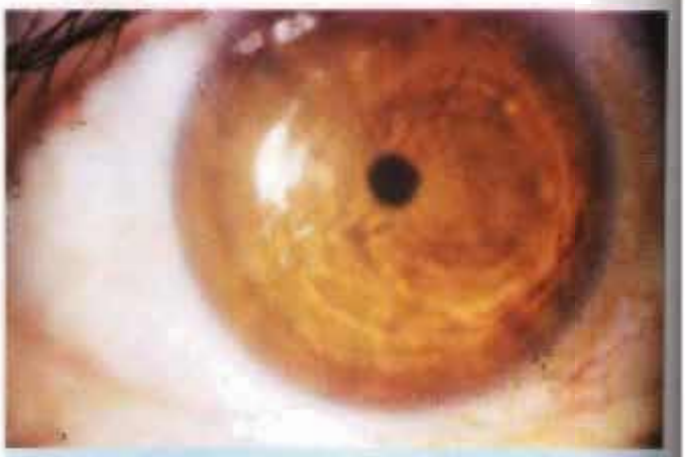

Fig. 6.22
Wrinkled flap following LASIK (Courtesy of H. Nano Jr)

CHAPTER 7

Episclera and Sclera

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Applied anatomy

The scleral stroma is composed of collagen bundles of varying size and shape that are not as uniformly orientated as in the cornea. The inner layer of the sclera (lamina fusca) blends with the suprachoroidal and supraciliary lamellae of the uveal tract. Anteriorly the episclera consists of a dense, vascular connective tissue which lies between the superficial scleral stroma and Tenon capsule. The three vascular layers that cover the anterior sclera are as follows:

1. **The conjunctival vessels** are the most superficial; arteries are tortuous and veins straight.
2. **The vessels within Tenon capsule** are straight with a radial configuration (Fig. 7.1a). In episcleritis, maximal congestion occurs within this vascular plexus (Fig. 7.1b), which can be manually moved over the sclera. Tenon capsule and the episclera are infiltrated with inflammatory cells, but the sclera itself is not swollen. Instillation of topical phenylephrine will cause blanching of the conjunctiva, and to a certain extent the Tenon vessels, allowing visualization of the underlying sclera.
3. **The deep vascular plexus** lies in the superficial part of the sclera and shows maximal congestion in scleritis (Fig. 7.1c). There is also inevitably some engorgement of the superficial vessels, but this should be ignored. Topical phenylephrine has no effect on the engorgement of these vessels. Examination in daylight is important to localize the level of maximal injection. The scleral stroma is largely avascular.

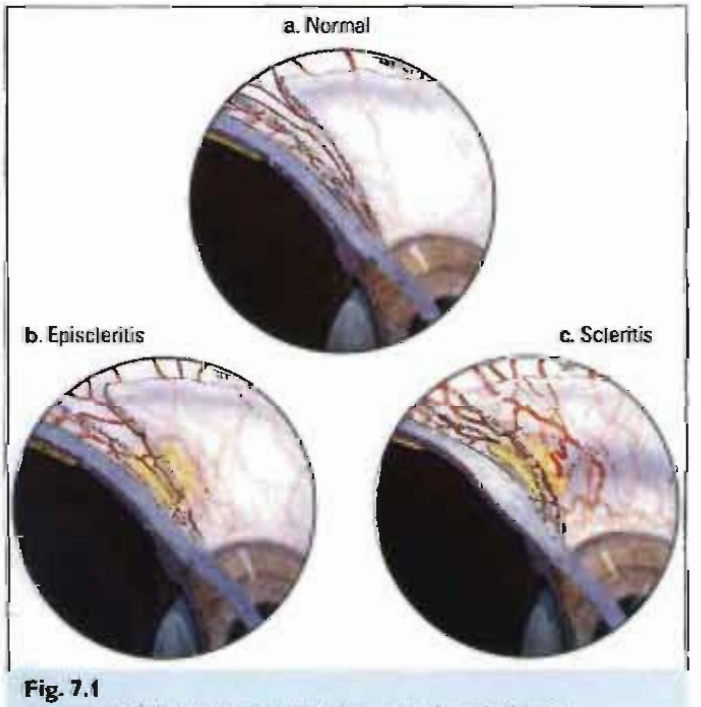

Fig. 7.1
Anatomy of the anterior vascular coats in relation to episcleritis and scleritis

Episcleritis

Episcleritis is a common, benign, self-limiting and frequently recurrent disorder which typically affects young adults. It may on occasion be associated with underlying systemic disease but never progresses to true scleritis. Episcleritis may be (a) *simple* or (b) *nodular*.

Clinical features

1. **Presentation** is with unilateral redness associated with mild discomfort, tenderness and watering.
2. **Signs**
   a. ***Simple episcleritis***, the commonest type, is characterized by sectoral (Fig. 7.2), or less commonly, diffuse

Fig. 7.2
Simple sectoral episcleritis

Fig. 7.3
Simple diffuse episcleritis

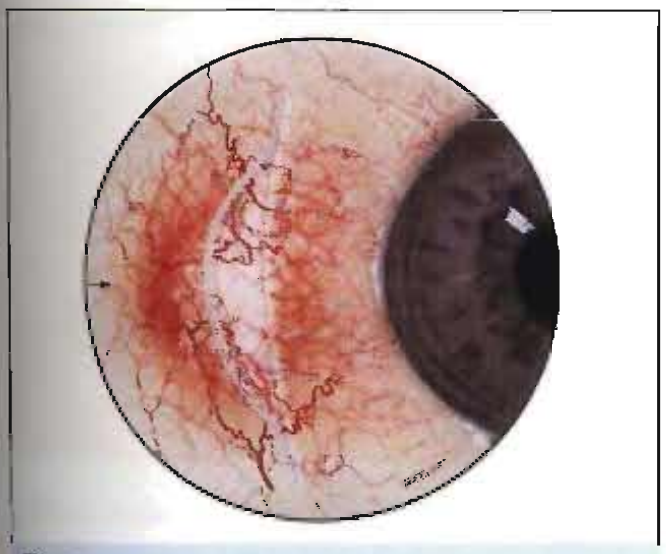

Fig. 7.4
Nodular episcleritis (Courtesy of P. Watson)

Fig. 7.5
Scleral translucency following recurrent episcleritis

redness (Fig. 7.3). It usually resolves spontaneously within 1–2 weeks.

b. Nodular episcleritis is characterized by a localized, raised, congested nodule which takes longer to resolve.

- A thin slit-lamp section shows that the anterior scleral surface is not raised, indicating that the sclera is not swollen (Fig. 7.4).
- Following recurrent attacks, the superficial scleral lamellae may become rearranged into more parallel rows, making the sclera appear more translucent (Fig. 7.5). This should not be mistaken for scleral thinning.

Treatment

This is not always required unless symptoms dictate otherwise.

1. **Simple lubricants** or vasoconstrictors suffice in most mild cases.
2. **Topical steroids** may be helpful but their use may result in recurrences. Frequent intensive instillation on a short-term pulsed basis is recommended.
3. **Oral non-steroidal anti-inflammatory drugs** (NSAIDs) such as flurbiprofen 100 mg t.i.d. for a few days may be required for severe recurrent or prolonged inflammation.

Scleritis

Scleritis is characterized by oedema and cellular infiltration of the entire thickness of the sclera. It is much less common than episcleritis and covers a spectrum ranging from trivial self-limiting episodes to a necrotizing process that may involve adjacent tissues and threaten vision.

Causes and associations

1. **Systemic associations** are present in about 50% of patients. Rheumatoid arthritis is by far the most common, followed by Wegener granulomatosis, relapsing polychondritis and polyarteritis nodosa (*see* Chapter 20).
2. **Surgically induced** scleritis follows ocular surgery. The exact aetiology is unknown but it has a strong association with underlying systemic disease and is more common in females. It typically presents within 6 months post-operatively as a focal area of intense inflammation and necrosis adjacent to the surgical site (Figs 7.6, 7.7).
3. **Infectious** scleritis is most frequently caused by spread of infection from a corneal ulcer. It may also be associated with trauma or follow excision of a pterygium with adjunctive beta irradiation or mitomycin C. The most frequent causative organisms are *Pseudomonas aeruginosa*, *Strep. pneumoniae*, *Staph. aureus* and Varicella zoster virus. Pseudomonal infection is difficult to treat and carries a poor prognosis. Fungal scleritis is very rare (Fig. 7.8).

Anatomical classification

This is based on the primary anatomical site of inflammation and associated vascular changes.

1. **Anterior scleritis** (98%)
   a. Non-necrotizing (85%): diffuse or nodular.
   b. Necrotizing (13%): with or without inflammation.
2. **Posterior scleritis** (2%)

Anterior non-necrotizing scleritis

Clinical features

1. **Presentation** is similar to episcleritis although discomfort may be more severe.

Fig. 7.6
Scleritis following scleral buckling for retinal detachment

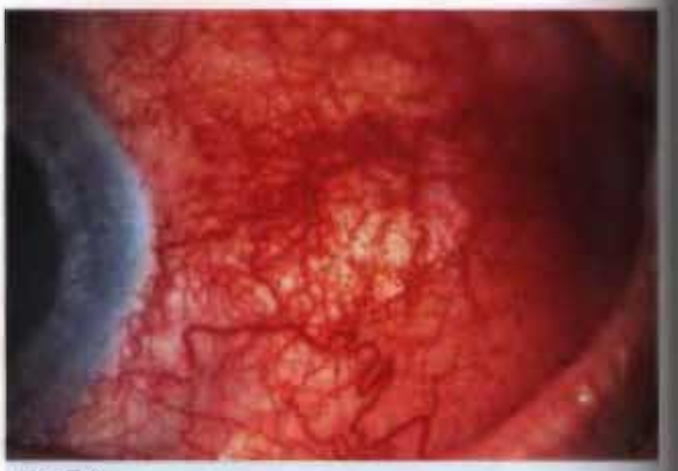

Fig. 7.9
Diffuse non-necrotizing anterior scleritis

Fig. 7.7
Scleritis following glaucoma filtration surgery

Fig. 7.10
Nodular non-necrotizing anterior scleritis

Fig. 7.8
Fungal scleritis (Courtesy of C. Barry)

2. Signs

*a. **Diffuse scleritis*** is characterized by widespread inflammation involving a sector or the entire anterior sclera. Distortion of the normal radial vascular pattern is characteristic (Fig. 7.9). The condition is relatively benign and neither progresses to the nodular type nor becomes necrotizing.

*b. **Nodular scleritis*** (Fig. 7.10) may, on cursory examination, resemble nodular episcleritis. However, the scleral nodule cannot be moved over the underlying tissue. Nodular disease is of intermediate severity with an overall incidence of visual impairment of about 25%.

Treatment

1. **Oral NSAIDs** such as flurbiprofen 100 mg t.i.d. or meloxicam 7.5 mg t.i.d. is the initial treatment.
2. **Oral prednisolone** 40–80 mg daily may be required as short-term therapy in patients resistant to or intolerant of NSAIDs.
3. **Combined therapy** with an NSAID and lower dose of steroid may be effective in the few patients who respond inadequately to either drug alone.

4. **Subconjunctival steroid injection** with triamcinolone acetonide (40 mg/ml) is a safe and effective alternative to systemic therapy but only for *non-necrotizing disease*.

Anterior necrotizing scleritis with inflammation

This is the most severe and distressing form of scleritis. It is bilateral in 60% of cases but involvement is not necessarily simultaneous. Most patients have an associated systemic vascular disease with a mortality rate of 25% within 5 years of the onset of scleritis. The visual prognosis is also poor.

Clinical features

1. **Presentation** is with gradual onset of pain and localized redness. The pain becomes severe and persistent and radiates to the temple, brow or jaw. It frequently interferes with sleep and responds poorly to analgesia.
2. **Signs** (in chronological order)
   - Congestion of the deep vascular plexus (Fig. 7.11).
   - Vascular distortion and occlusion, with resultant avascular patches (Fig. 7.12).
   - Scleral necrosis which may be associated with overlying conjunctival ulceration (Fig. 7.13).
   - Gradual spread of necrosis which may coalesce with other separate necrotic areas (Fig. 7.14).
   - Upon resolution a bluish tinge appears due to increased visibility of underlying uvea secondary to scleral thinning (Fig. 7.15).

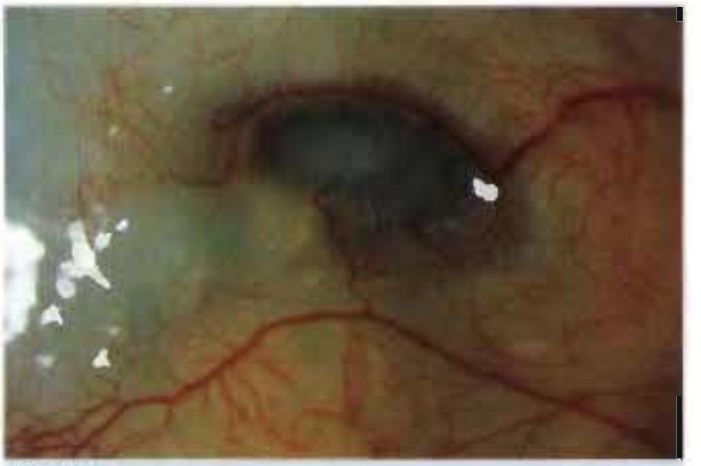

Fig. 7.13
Patch of scleral necrosis in anterior necrotizing scleritis with inflammation

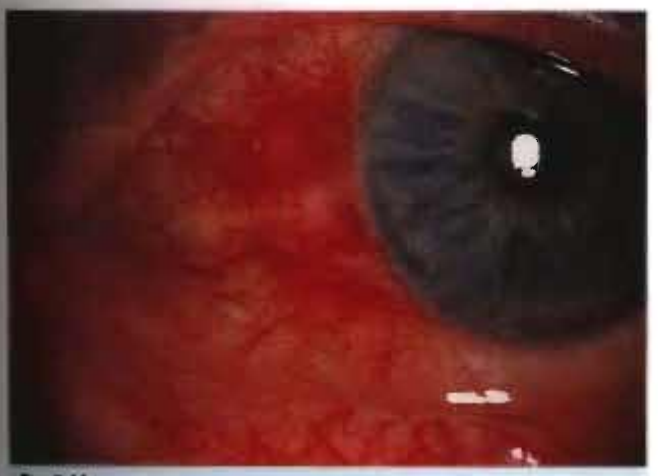

Fig. 7.11
Deep vascular congestion in early anterior necrotizing scleritis with inflammation

Fig. 7.14
Advanced anterior necrotizing scleritis with inflammation (Courtesy of P. Watson)

Fig. 7.12
Avascular patch in anterior necrotizing scleritis with inflammation (Courtesy of P. Watson)

Complications

1. **Staphyloma formation** (Fig. 7.16), and occasionally perforation, may occur secondary to severe scleral

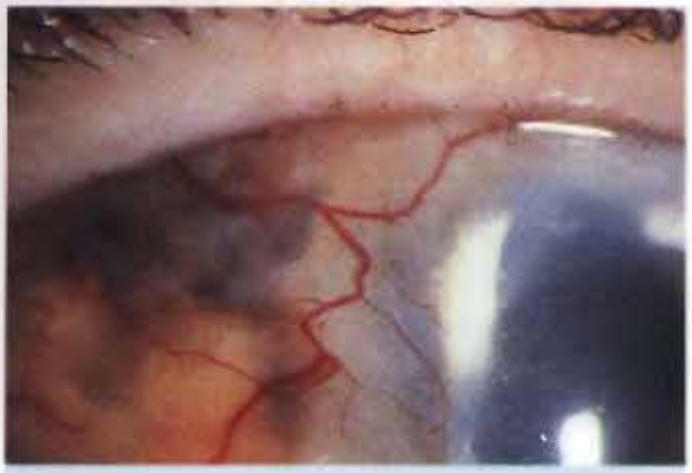

Fig. 7.15
Uveal visibility due to scleral thinning in resolved anterior necrotizing scleritis with inflammation

thinning, particularly if the intraocular pressure is elevated.

2. **Anterior uveitis** reflects extension of inflammation to the uvea in severe disease. Long-standing uveitis may result in secondary cataract, glaucoma and macular oedema. It is therefore important to detect and treat uveitis promptly. In general, the prognosis is poor with a high incidence of visual impairment.

Treatment

1. **Oral prednisolone** 60–120 mg daily for 2–3 days usually has a dramatic effect on the severity of pain, which is an important indicator of active disease. The dose can then be tapered accordingly.
2. **Immunosuppressive agents** (cyclophosphamide, azathioprine or cyclosporin) may be necessary in steroid-resistant cases.

Fig. 7.16
Scleral staphyloma due to anterior necrotizing scleritis with inflammation

Fig. 7.18
Advanced scleromalacia perforans

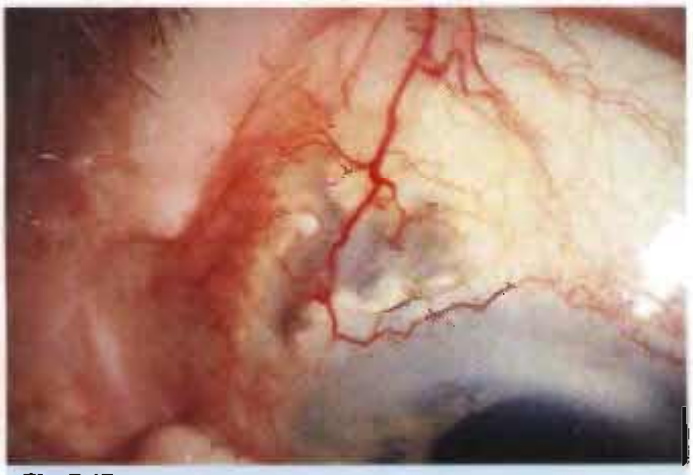

Fig. 7.17
Early scleromalacia perforans

Fig. 7.19
Scleral staphyloma in severe scleromalacia perforans

3. **Combined therapy** (pulsed intravenous methylprednisolone 500–1000 mg and cyclophosphamide 500 mg) is reserved for the minority of patients who fail to resolve with oral therapy or those who present with established scleral necrosis.

Anterior necrotizing scleritis without inflammation

Also known as scleromalacia perforans, this typically occurs in women with long-standing rheumatoid arthritis and is usually bilateral.

1. **Signs** (in chronological order)
   - Asymptomatic yellow necrotic scleral patches in uninflamed sclera.
   - Enlargement, spread and coalescence.
   - Progressive exposure of underlying uvea as a result of scleral thinning (Figs 7.17, 7.18).
   - Staphyloma formation (Fig. 7.19) may occur but spontaneous perforation is rare unless the intraocular pressure is elevated.
2. **Treatment** is ineffective.

Posterior scleritis

Posterior scleritis is uncommon and often misdiagnosed because it may present with a range of clinical findings which may be confused with other inflammatory and neoplastic conditions. The condition affects women twice as often as men and one-third of patients are under 40 years of age at presentation. Patients over 50 years are at increased risk of harbouring a systemic disease and suffering visual loss. Two-thirds of cases have unilateral involvement. There is no correlation between unilateral and bilateral cases and systemic disease or visual loss. In general the visual prognosis is guarded and about one-third of patients develop visual impairment to some degree.

Fig. 7.21
Exudative retinal detachment and ring choroidal detachments in posterior scleritis

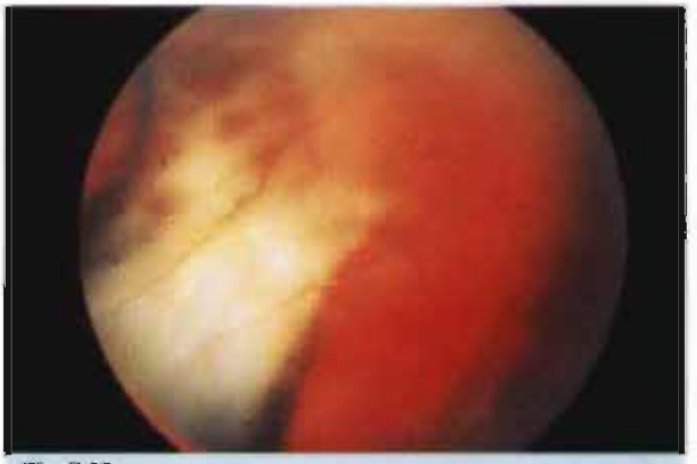

Fig. 7.22
Subretinal lipid exudation in posterior scleritis (Courtesy of P. Watson)

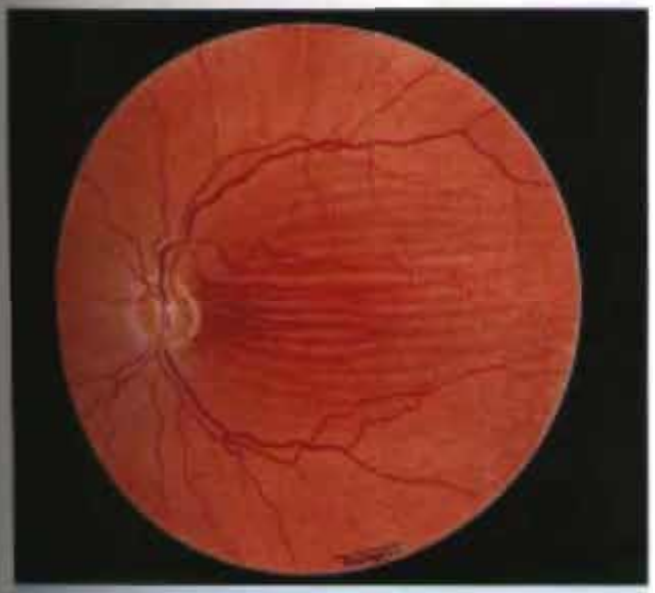

Fig. 7.20
Choroidal folds in posterior scleritis

1. **Presentation** is variable and depends on the exact site of involvement. The most common symptoms are pain and visual impairment.
2. **Signs**
   a. ***External*** signs include lid oedema and fullness, proptosis and ophthalmoplegia. Associated anterior scleritis is present in about one-third of cases.
   b. ***Fundus*** findings include disc swelling, macular oedema, choroidal folds (Fig. 7.20), exudative retinal

Fig. 7.23
Ultrasonogram in severe posterior scleritis showing scleral thickening and fluid in sub-Tenon space

Fig. 7.24
CT scan in right posterior scleritis showing scleral thickening and mild proptosis

detachment, ring choroidal detachments (Fig. 7.21) and subretinal lipid exudation (Fig. 7.22).

3. **Investigations**
   a. *Ultrasonography* shows thickening of the posterior sclera and fluid in Tenon space giving rise to the characteristic 'T' sign. The stem of the T is formed by the optic nerve on its side and the cross bar by the gap containing fluid in sub-Tenon space (Fig. 7.23).
   b. *CT* demonstrates posterior scleral thickening (Fig. 7.24).
4. **Differential diagnosis** includes optic neuritis, rhegmatogenous retinal detachment, choroidal tumour, orbital inflammatory disease or mass, uveal effusion syndrome, Harada disease and intraocular lymphoma.
5. **Treatment** in elderly patients with associated systemic disease is as for necrotizing anterior scleritis. Young patients without associated systemic disease usually respond well to NSAIDs.

Scleral discoloration

Focal discoloration

This is usually seen anterior to the insertions of the horizontal recti and may be caused by the following:

1. **Senile scleral translucency** which is characterized by oval, dark-greyish areas (Fig. 7.25).
2. **Alkaptonuria** may cause brown-black discoloration (ochronosis) at the insertions of horizontal recti and pigmentation of the pinnae.
3. **Haemochromatosis** causes rusty-brown discoloration.
4. **Systemic minocycline** may cause blue-grey paralimbal discoloration, usually denser in the interpalpebral area, possibly due to the photosensitizing properties of the drug. This may be associated with pigmentation of skin, teeth, nails, mucosa, thyroid and bones.
5. **Metallic foreign body**, if long-standing, may produce rust staining.

Fig. 7.25
Senile scleral translucency

Fig. 7.26
Blue sclera

Diffuse discoloration

1. **Yellow** discoloration is caused by jaundice.
2. **Blue** discoloration is caused by thinning and transparency of scleral collagen with visualization of the underlying uvea (Fig. 7.26). Important causes include osteogenesis imperfecta types 1 and 2, Ehlers–Danlos syndrome (usually type 6), pseudoxanthoma elasticum (dominant type 2) and Turner syndrome.

CHAPTER 8

Lens

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Introduction

The crystalline lens is a biconvex, avascular, transparent structure enclosed by a capsule, a basement membrane secreted by the lens epithelium. The capsule, responsible for moulding the lens substance during accommodation, is thickest in the equatorial zone and thinnest at the posterior pole of the lens. A ring of zonular fibres, which insert in the equatorial region, suspends the lens from the ciliary body. A monolayer of epithelium lines only the anterior and equatorial lens capsule. Cells in the equatorial region exhibit mitotic activity. Newly formed epithelial cells elongate to form fibres, which lose their organelles, thus optimizing lens transparency. Lens substance may be conceptualized as consisting of the nucleus, the central compacted core, which is surrounded by the cortex. New lens fibres are continuously laid down subcapsularly throughout life, resulting in the older layers acquiring progressively deeper localizations within the lens substance. The lens thus grows, in both anteroposterior and equatorial dimensions, throughout life. The normal lens is transparent; any congenital or acquired opacity in the lens capsule or substance, irrespective of the effect on vision, is a cataract.

Acquired cataract

Age-related cataract

Morphological classification

1. **Subcapsular cataract**
   a. *Anterior subcapsular* cataract lies directly under the lens capsule and is associated with fibrous metaplasia of the lens epithelium (Fig. 8.1).
   b. *Posterior subcapsular* cataract lies just in front of the posterior capsule and manifests a vacuolated, granular or plaque-like appearance (Fig. 8.2). Due to its location at the nodal point of the eye, a posterior subcapsular opacity has a more profound effect on vision than a comparable nuclear or cortical cataract. Patients are particularly troubled under conditions of miosis, such as produced by headlights of oncoming cars and bright sunlight. Near vision is also frequently impaired more than distance vision.
2. **Nuclear** cataract starts as an exaggeration of the normal ageing changes involving the lens nucleus (Fig. 8.3). It is often associated with myopia due to an increase in the refractive index of the lens nucleus and also with increased spherical aberration. Some elderly patients may consequently be able to read again without spectacles ('second sight of the aged'). Nuclear sclerosis is characterized in its early stages by a yellowish hue due to the deposition of urochrome pigment (Fig. 8.4). When advanced the nucleus appears brown (a brunescent cataract) (Fig. 8.5). Such cataracts are of hard consistency, which is surgically relevant.
3. **Cortical** cataract may involve the anterior, posterior or equatorial cortex. The opacities start as clefts (Fig. 8.6)

Fig. 8.1
Anterior subcapsular cataract

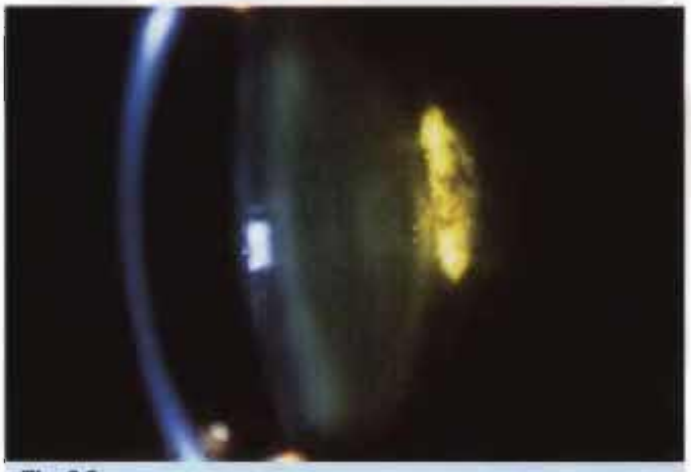

Fig. 8.2
Posterior subcapsular cataract

Fig. 8.3
Early nuclear cataract

Fig. 8.4
Moderate nuclear cataract

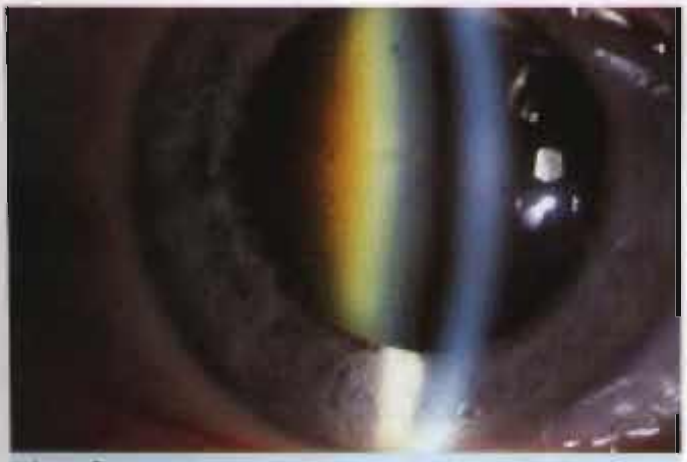

Fig. 8.5
Brunescent nuclear cataract

Fig. 8.6
Cortical clefts

Fig. 8.7
Cortical vacuoles

Fig. 8.8
Advanced cortical cataract

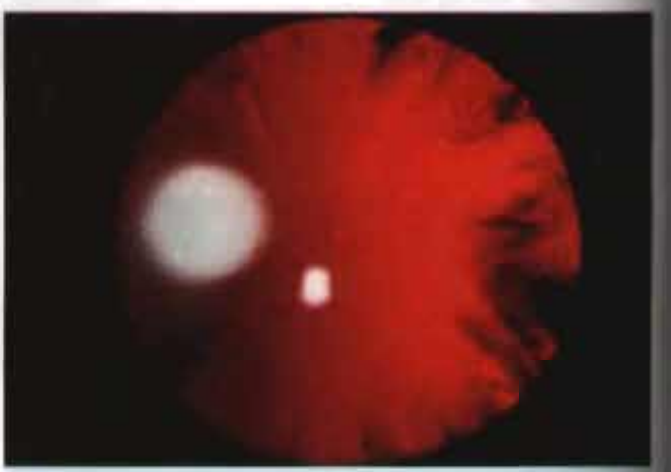

Fig. 8.9
Cortical cataract seen on retroillumination

and vacuoles (Fig. 8.7) between lens fibres due to hydration of the cortex. Subsequent opacification results in typical cuneiform (wedge-shaped) or radial spoke-like opacities, often initially in the inferonasal quadrant. Both cortical and subcapsular cataracts are white on oblique illumination (Fig. 8.8) and appear black, silhouetted against the red reflex, on retroillumination (Fig. 8.9).

4. **Christmas tree** cataract, which is uncommon, is characterized by striking, polychromatic, needle-like deposits in the deep cortex and nucleus which may be solitary (Fig. 8.10) or associated with other opacities (Fig. 8.11).

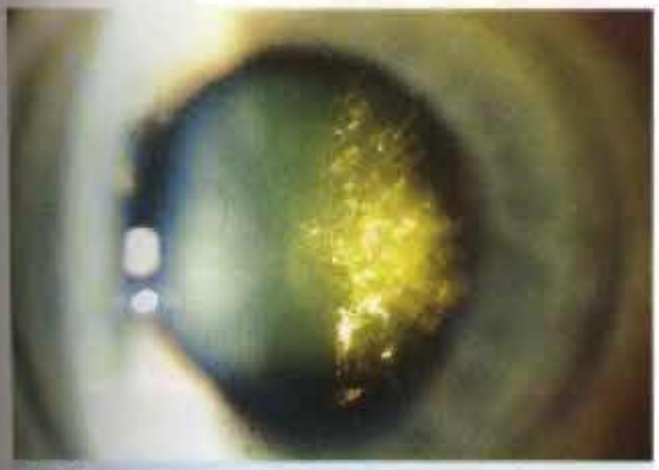

Fig. 8.10
Christmas tree cataract

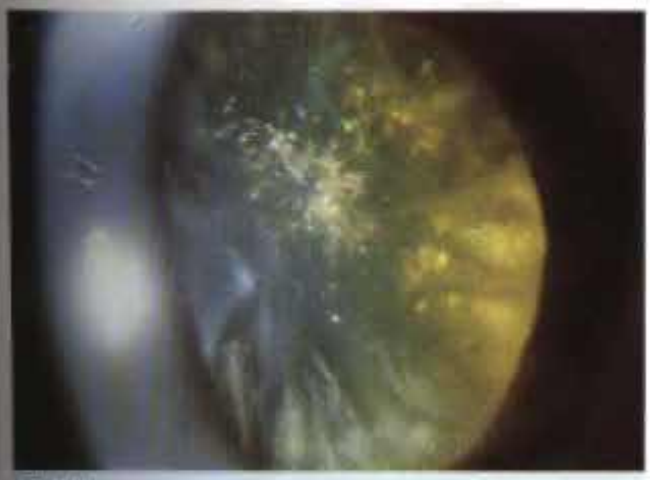

Fig. 8.11
Mixed christmas tree and cortical cataract

Fig. 8.12
Mature cataract

Classification according to maturity

1. **An immature** cataract is one in which the lens is partially opaque.
2. **A mature** cataract is one in which the lens is completely opaque (Fig. 8.12).
3. **A hypermature** cataract has a shrunken and wrinkled anterior capsule due to leakage of water out of the lens (Fig. 8.13).
4. **A morgagnian** cataract is a hypermature cataract in which total liquefaction of the cortex has allowed the nucleus to sink inferiorly (Fig. 8.14).

Presenile cataract

Cataract may develop early in the following conditions:

1. **Diabetes mellitus** (*see* Chapter 20), in addition to causing cataract, can affect the refractive index of the lens and also its amplitude of accommodation.
   a. ***Classical diabetic*** cataract is rare. Hyperglycaemia is reflected in a high level of glucose in the aqueous

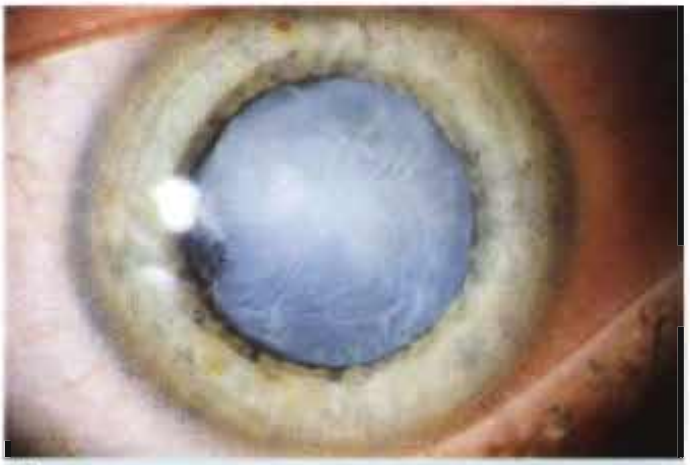

Fig. 8.13
Hypermature cataract with wrinkling of the anterior capsule

Fig. 8.14
Morgagnian cataract

Fig. 8.15
Diabetic snowflake cataract (Courtesy of A. Fielder)

humour, which diffuses into the lens. Here glucose is metabolized by aldose reductase into sorbitol, which then accumulates within the lens, resulting in secondary osmotic overhydration of the lens substance. In mild degree, this may affect the refractive index of the lens with consequent fluctuation of refraction *pari passu* with the plasma glucose level (hyperglycaemia resulting in myopia). Cortical fluid vacuoles develop and later evolve into frank opacities. Classical diabetic cataract consists of snowflake cortical opacities (Fig. 8.15) occurring in the young diabetic. Such a cataract may resolve spontaneously or mature within a few days.

*b. **Age-related*** cataract occurs earlier in diabetes mellitus. Nuclear opacities are common and tend to progress rapidly.

*c. **Premature presbyopia*** may be seen due to reduced pliability of the lens.

2. **Myotonic dystrophy** (*see* Chapter 20). About 90% of patients develop visually innocuous, fine cortical iridescent opacities in the third decade, which evolve into visually disabling stellate posterior subcapsular cataract by the fifth decade (Fig. 8.16). Occasionally cataract may antedate myotonia.
3. **Atopic dermatitis** (*see* Chapter 20). About 10% of patients with severe atopic dermatitis develop cataracts in the second to fourth decades. The opacities are often bilateral and may mature quickly.
   *a. **Shield-like*** dense anterior subcapsular plaque which wrinkles the anterior capsule is characteristic (Fig. 8.17).
   *b. **Posterior subcapsular*** opacities resembling a complicated cataract may also occur.
4. **Neurofibromatosis type 2** (*see* Chapter 20) is associated with posterior subcapsular or posterior cortical opacities.

Fig. 8.17
Shield-like anterior subcapsular cataract in atopic dermatitis

Traumatic cataract

Trauma is the most common cause of unilateral cataract in young individuals. The following may be responsible:

1. **Direct penetrating** injury to the lens (Fig. 8.18).
2. **Concussion** may cause an 'imprinting' of iris pigment on the anterior lens capsule (Vossius ring) (Fig. 8.19) as well

Fig. 8.16
Stellate posterior subcapsular cataract in myotonic dystrophy seen on retroillumination

Fig. 8.18
Cataract caused by penetrating trauma

Fig. 8.19
Vossius ring due to blunt trauma

Fig. 8.20
Flower-shaped (rosette) cataract due to blunt trauma

as striking flower-shaped cortical opacities (rosette cataract) (Fig. 8.20).

3. **Electric shock** and **lightning** are rare causes.
4. **Ionizing radiation** to ocular tumours.
5. **Infrared radiation**, if intense as in glassblowers, may rarely cause true exfoliation or lamellar delamination of the anterior lens capsule in which the superficial portion of a thickened capsule splits from the deeper layer and extends into the anterior chamber. This condition is distinct from pseudoexfoliation in which fibrillary material is deposited on the anterior lens surface and other ocular structures (*see* Chapter 9).

Drug-induced cataract

1. **Steroids**, both systemic and topical, are cataractogenic. The lens opacities are initially posterior subcapsular; later the anterior subcapsular region becomes affected. The relationship between weekly systemic dose, duration of administration, total dose and cataract formation is unclear. It is thought that patients on less than 10 mg prednisolone (or equivalent), or treated for less than 4 years, may be immune. Although it is believed that children may be more susceptible to the cataractogenic effects of systemic steroids, individual (genetic) susceptibility may also be of relevance. It has therefore been suggested that the concept of a safe dose be abandoned. Patients who develop lens changes should have their dosage reduced to a minimum consistent with control of the underlying disease, and if possible be considered for alternate-day therapy. Early opacities may regress if therapy is discontinued; alternatively progression may occur despite withdrawal and warrant surgical intervention.
2. **Chlorpromazine** may cause the deposition of innocuous, fine, stellate, yellowish-brown granules on the anterior lens capsule within the pupillary area (Fig. 8.21). Diffuse, granular deposits on the corneal endothelium and in the deep stroma may also occur. Both lenticular and corneal deposits are dose-related and usually irreversible. In very high doses (>2400 mg daily) this drug may cause retinotoxicity (*see* Chapter 13).
3. **Busulphan** (Myleran), used in the treatment of chronic myeloid leukaemia, may occasionally cause lens opacities.

Fig. 8.21
Anterior lens deposits due to the long-term use of chlorpromazine

4. **Amiodarone**, used in the treatment of cardiac arrhythmias, causes visually inconsequential anterior subcapsular lens deposits in about 50% of patients on moderate to high doses. Vortex keratopathy may also occur (*see* Chapter 5).
5. **Gold**, used in the treatment of rheumatoid arthritis, causes innocuous anterior capsular deposits in about 50% of patients on treatment for longer than 3 years.
6. **Allopurinol**, used in the treatment of hyperuricaemia and chronic gout, increases the risk of cataract formation in elderly patients, if the cumulative dose exceeds 400 g or duration of administration exceeds 3 years.

Fig. 8.22
Posterior polychromatic lustre in chronic anterior uveitis

Fig. 8.23
Anterior cataract and extensive posterior synechiae in chronic anterior uveitis

Fig. 8.24
Mature cataract and posterior synechiae in chronic anterior uveitis

Secondary cataract

A secondary (complicated) cataract develops as a result of some other primary ocular disease.

1. **Chronic anterior uveitis** is the most common cause of secondary cataract. The earliest finding is a polychromatic lustre at the posterior pole of the lens (Fig. 8.22) which may not progress if the uveitis is arrested. If the inflammation persists, posterior and anterior opacities develop (Fig. 8.23) and may progress to maturity (Fig. 8.24). Lens opacities appear to progress more rapidly in the presence of posterior synechiae.
2. **Acute congestive angle-closure glaucoma** may cause small, grey-white, anterior, subcapsular or capsular opacities within the pupillary area (glaukomflecken) (Fig. 8.25). They represent focal infarcts of the lens epithelium and are pathognomonic of past acute angle-closure glaucoma.
3. **High (pathological) myopia** is associated with posterior subcapsular lens opacities and early-onset nuclear sclerosis, which may ironically increase the myopic refractive error. Simple myopia, however, is not associated with such cataract formation.
4. **Hereditary fundus dystrophies** such as retinitis pigmentosa, Leber congenital amaurosis, gyrate atrophy and Stickler syndrome may be associated with posterior subcapsular lens opacities (*see* Chapter 15). Cataract surgery may occasionally improve visual acuity even in the presence of severe retinal changes.

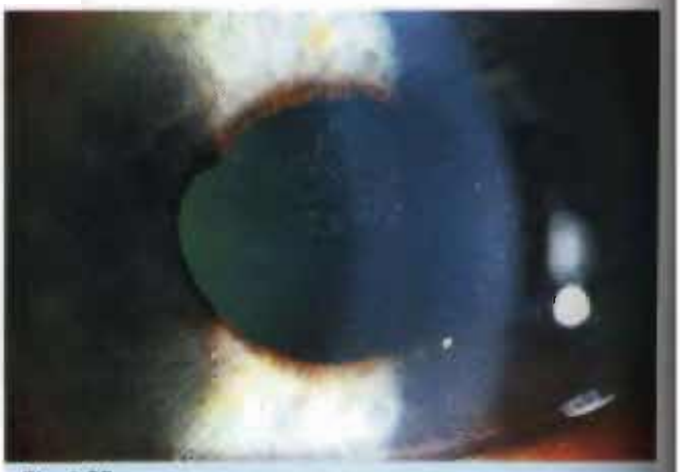

Fig. 8.25
Anterior capsular cataract following acute angle-closure glaucoma (glaukomflecken)

Management of age-related cataract

Introduction

Indications for surgery

1. **Visual improvement** is by far the most common indication for cataract surgery, although requirements vary from person to person. Surgery is indicated only if and when cataract develops to a degree sufficient to cause difficulty in performing daily essential activities. If the

patient desires to drive or continue a specific occupation, visual function below legally prescribed levels may necessitate cataract surgery.

2. **Medical indications** are those in which a cataract is adversely affecting the health of the eye, for example, phacolytic glaucoma or phacomorphic glaucoma (*see* Chapter 9). Cataract surgery to improve the clarity of the ocular media may also be required in the context of fundal pathology (e.g. diabetic retinopathy) requiring monitoring or treatment with laser photocoagulation.
3. **Cosmetic indications** are rare, such as when a mature cataract in an otherwise blind eye is removed to restore a black pupil.

Preoperative evaluation

Apart from a general medical examination, a patient due to undergo cataract surgery requires a detailed and pertinent ophthalmic examination, with special regard to the following:

1. **Cover test.** A heterotropia may indicate amblyopia, which carries a guarded visual prognosis, or the possibility of diplopia if the vision is improved.
2. **Pupillary responses.** Because a cataract never produces an afferent pupillary defect, its presence implies additional pathology, which may influence the final visual outcome.
3. **Ocular adnexa.** Dacryocystitis, blepharitis, chronic conjunctivitis, lagophthalmos, ectropion, entropion and tear film abnormalities may predispose to endophthalmitis and require effective preoperative treatment.
4. **Cornea.** A wide arcus senilis or stromal opacities may prejudice a good surgical view. Guttata indicate endothelial dysfunction and consequent vulnerability to decompensation secondary to operative trauma.
5. **Anterior segment.** A shallow anterior chamber can render cataract surgery difficult. Pseudoexfoliation indicates a weak zonule, with the possibility of problems during surgery. A poorly dilating pupil can make cataract surgery difficult. Recognition of this allows intensive preoperative mydriatic drops or planned stretching of the pupil prior to capsulorhexis. A poor red reflex compromises the performance of a good capsulorhexis. This can be overcome by staining the capsule with a dye such as trypan blue.
6. **Lens.** The type of cataract is relevant. Nuclear cataracts tend to be hard and require more phaco power, while cortical and subcortical cataracts tend to be softer.
7. **Intraocular pressure.** Any glaucoma or ocular hypertension must be noted.
8. **Fundus.** Recognition of fundal pathology such as age-related macular degeneration, which may affect the visual outcome.

Biometry

Surgical removal of the crystalline lens subtracts approximately 20 D from the refracting system of the eye. The aphakic eye is grossly hypermetropic; modern cataract surgery therefore involves the implantation of an intraocular lens (IOL), ideally in the same location as the surgically removed crystalline lens. Biometry affords calculation of the lens power likely to result in emmetropia or, alternatively, a desired postoperative refractive error. In its simplest form, biometry involves two ocular parameters: (a) *keratometry*—the curvature of the anterior corneal surface (steepest and flattest meridians), expressed in dioptres or millimetres of radius of curvature and (b) *axial length*—the anteroposterior dimension of the eye in millimetres, measured on A-scan ultrasonography.

1. **SRK formula.** Perhaps the most commonly used mathematical formula to calculate IOL power is that developed by Sanders, Retzlaff and Kraff which states that $P = A - 2.5L - 0.9K$
   - P is the lens power required to generate postoperative emmetropia.
   - A is the A constant, which varies (between 114 and 119) with different IOLs.
   - L is the axial length in millimetres.
   - K is the average keratometry reading in dioptres.

   Numerous other formulae, incorporating additional parameters such as anterior chamber depth and individualized surgeon factors have been developed to optimize the accuracy of preoperative prediction.
2. **Postoperative refraction.** Emmetropia is perhaps the ideal postoperative refraction, with spectacles needed only for close work (since an IOL cannot accommodate). In practice, most surgeons aim for a small degree of myopia (about 0.25 D) to offset possible error in biometry. This is because a slight degree of myopia is acceptable in most patients, and may even be advantageous, while postoperative hypermetropia, which necessitates spectacles for clear vision at all distances, is poorly tolerated. The planning of postoperative refraction also needs to take account of the other eye. If the other eye has clear vision with a significant refractive error and is unlikely to require surgery, then postoperative refraction should be targeted at within 2 D of the other eye, to avoid problems with binocular coordination.

Anaesthesia

Evidence for the benefit of local anaesthesia (LA) over general anaesthesia (GA) for most intraocular procedures is sparse. The choice is generally determined by patient preference and the clinical judgement of the surgical team. Day-case cataract surgery under LA is safe and generally preferred by patients and staff alike. It affords significant economic benefits and is the option of choice.

1. **Retrobulbar block** is given into the muscle cone behind the globe close to the ciliary ganglion with a 1.5 inch (38 mm) needle. It also provides akinesia so that ocular movements are greatly decreased or eliminated altogether. Retrobulbar injection requires considerable skill and experience and is occasionally associated with serious

complications such as orbital haemorrhage, penetration of the globe, intravascular injection, damage to the optic nerve and brain stem anaesthesia. Temporary problems include ptosis and diplopia. Retrobulbar anaesthesia often requires a separate facial block to paralyse the orbicularis oculi.

2. **Peribulbar block** is given through the skin or conjunctiva with a 1 inch (25 mm) needle. More than one injection and a greater volume of anaesthetic agent is required compared with retrobulbar block. Because the needle is shorter the risk of brain stem anaesthesia is reduced although haemorrhage and ocular penetration may occur.
3. **Parabulbar (sub-Tenon) block** involves passing a blunt-tipped cannula through an incision in the conjunctiva and Tenon capsule 5 mm from the limbus, and along the sub-Tenon space. The anaesthetic is injected beyond the equator of the globe. Although anaesthesia is good and complications minimal, akinesia is variable.
4. **Topical–intracameral anaesthesia** involves initial surface anaesthesia with drops or gel (proxymetacaine 0.5%, lignocaine 4%) and intracameral injection or infusion of diluted preservative-free anaesthetic.

Intraocular lenses

Basic aspects

1. **Positioning.** An IOL consists of the optic (the central refracting element) and the haptics, which sit in contact with the ocular structures (capsular bag, ciliary sulcus or anterior chamber angle), thus affording optimal and stable position (centration) of the optic. Modern cataract surgery, with preservation of the capsular 'bag', affords positioning of the IOL in the ideal location—'in the bag'. Complicated surgery, with rupture of the posterior capsule, may, however, necessitate alternative positioning of the IOL, in the posterior chamber (with haptics in the ciliary sulcus) or in the anterior chamber with the haptics supported in the chamber angle. The latter is designated an AC-IOL in contrast to the former two, which are PC-IOLs.
2. **Designs** are numerous and continue to evolve. The lenses may be rigid or flexible. A rigid IOL requires an incision larger than the diameter of the optic, often 5–6.6 mm, for insertion. A flexible IOL, however, may be folded with forceps or loaded into an injector/delivery system and inserted through a much smaller incision, often 2.5–3 mm. Haptics are made from polymethylmethacrylate (PMMA), polypropylene (Prolene) or polyamide and may be in the form of loops or plates. In a one-piece IOL the haptics and optic are made from the same material and have no joints; a three-piece IOL is characterized by optics and haptics from different materials, which necessarily are joined together. Optics may also be of different sizes and shapes. Conventional IOLs are monofocal; lately multifocal designs that allow clear vision at different distances are being developed.
3. **Rigid IOLs** are made entirely from PMMA. The composition of PMMA varies depending on the manufacturing process. Compression-moulded and lathe-cut IOLs require high-molecular-weight PMMA, while injection-moulded lenses need lower-molecular-weight PMMA. Modern rigid IOLs are one-piece to facilitate maximal stability and fixation.
4. **Foldable IOLs** are made from the following materials:
   a. *Silicone* IOLs, both three-piece loop and one-piece plate haptics, are associated with lower rates of posterior capsular opacification than PMMA lenses.
   b. *Acrylic* IOLs, three-piece or one-piece, may be hydrophobic (water content <1%) or hydrophilic (water content 18–35%). Certain acrylic IOLs inhibit opacification of the posterior capsule.
   c. *Hydrogel* IOLs are similar to hydrophylic acrylic IOLs have a high water content (38%) and are available as three-piece designs.
   d. *Collamer* IOLs, made from a mixture of collagen and hydrogel, have recently been introduced.

Cataract surgery

Principles

1. **Extracapsular cataract extraction** (ECCE) requires a relatively large circumferential limbal incision (8–10 mm) through which the lens nucleus is extracted and the cortical matter aspirated, leaving behind an intact posterior capsule. The IOL is then inserted.
2. **Phacoemulsification** (phaco) has become the preferred method of cataract extraction over the last decade. A fine hollow needle, usually titanium, attached to a handpiece containing a piezo-electric crystal, vibrates longitudinally at ultrasonic frequencies. The tip is applied to the lens nucleus; cavitation occurs at the tip as the nucleus is emulsified. An irrigating/aspiration system removes this emulsified material from the eye. The IOL is then inserted (if folded) or implanted through a much smaller incision than in ECCE. The smaller incision renders the operation safer, since decompression of the eye is avoided; this reduces the incidence of operative complications such as suprachoroidal haemorrhage. The following of the anterior chamber and vitreous prolapse in the event of rupture of the posterior capsule. In addition, the procedure is associated with little postoperative astigmatism and early stabilization of refraction (usually 3 weeks). Postoperative wound-related problems such as iris prolapse are almost eliminated.

Technique of extracapsular extraction

1. A circumferential vertical partial thickness incision is made in the peripheral clear cornea at the limbus and the anterior chamber entered with a keratome.
2. Viscoelastic substance such as sodium hyaluronate or hydroxymethylpropylcellulose is injected into the anterior chamber. This maintains the chamber and protects the corneal endothelium.

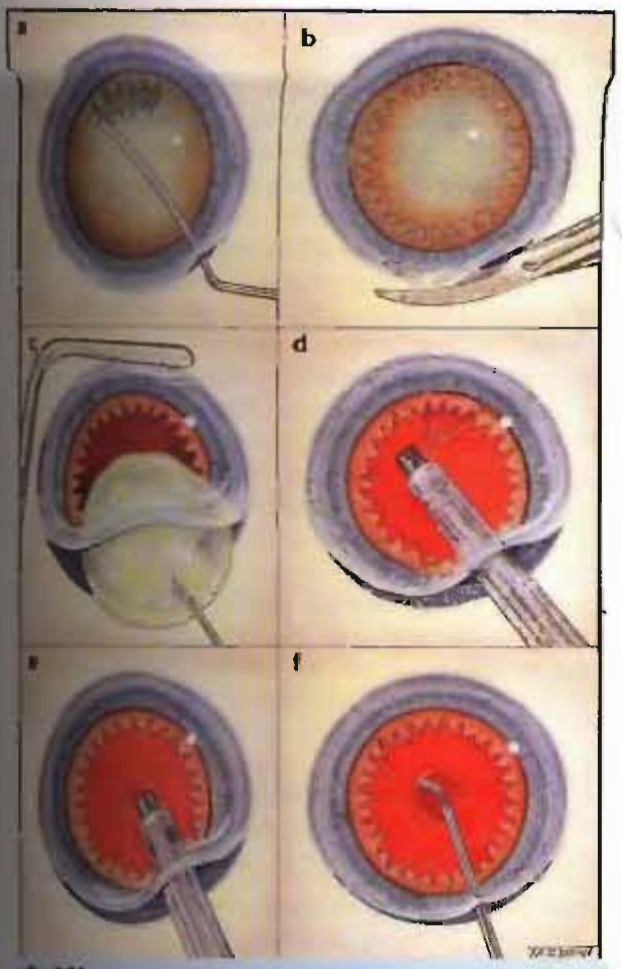

Fig. 8.26
Extracapsular cataract extraction (see text)

1. The cystitome is introduced into the anterior chamber and multiple small radial cuts are made in the anterior capsule for 360° (Fig. 8.26a). These cuts are then joined together to create a 'can-opener' capsulotomy. Alternatively, a capsulorhexis may be performed, which involves making a controlled circular tear in the capsule.
2. The limbal partial-thickness incision is completed with scissors (Fig. 8.26b).
3. Hydrodissection is performed by injecting balanced salt solution (BSS) with a special blunt-tipped (Rycroft) cannula between the edge of the capsule and the peripheral lens cortex in order to free the lens matter from the capsular bag.
4. The nucleus is expressed by applying pressure alternately at the superior and inferior limbus (Fig. 8.26c) or by manipulating it out with a vectis.
5. The tip of the infusion–aspiration cannula is introduced into the anterior chamber and passed under the lens capsule at 6 o'clock. Strands of cortex are engaged into the port by activating the suction mechanism (Fig. 8.26d).
6. The cortex is then dragged centrally and aspirated under direct visualization. This manoeuvre is repeated sequentially until all cortex has been removed. It is important not to inadvertently aspirate the posterior capsule because this may cause it to rupture, with numerous attendant complications. Aspiration of the capsule is indicated by the appearance of fine sharp lines radiating from the aspiration port (Fig. 8.26e). Aspiration should be immediately terminated and fluid reflux activated to disengage the capsule.
9. If necessary, the posterior capsule may be polished to remove any small residual subcapsular plaques (Fig. 8.26f).
10. Viscoelastic substance is injected into the capsular bag to facilitate subsequent insertion of the IOL (Fig. 8.27a).
11. The IOL is grasped by the optic and its anterior surface coated with viscoelastic substance (Fig. 8.27b).
12. The leading haptic is inserted through the lips of the incision and then passed under the lens capsule at 6 o'clock (Fig. 8.27c).
13. The tip of the superior haptic is grasped with forceps and advanced into the anterior chamber (Fig. 8.27d). As the superior pole of the haptic clears the edge of the pupil, the arm is pronated to ensure that on release the haptic will spring open under the iris and not out of the incision.

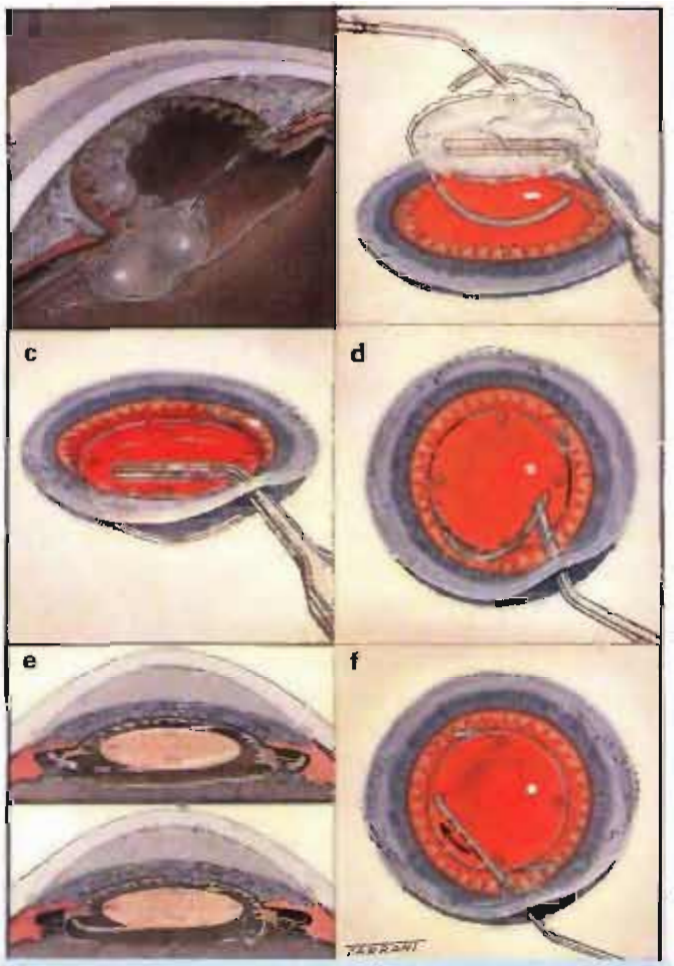

Fig. 8.27
Extracapsular cataract extraction (see text)

NB: Both haptics should preferably be placed in the capsular bag (Fig. 8.27e, bottom) rather than in the ciliary sulcus (Fig. 8.27e, top).

14. The IOL is dialled into the horizontal position by engaging the guide holes with a special hook (Fig. 8.27f).
15. The pupil is constricted by injecting Miochol (acetylcholine) into the anterior chamber, viscoelastic substance is aspirated, and the incision is sutured.

Phacoemulsification

The technique is constantly changing and there are many variations. The basic steps for a classic technique (4 quadrant 'divide and conquer') are as follows:

1. A self-sealing tunnel incision is made into the anterior chamber. This may be in clear peripheral cornea, preferably temporally, or via a scleral tunnel incision, usually superiorly.
2. Viscoelastic substance is injected into the anterior chamber.
3. A second stab incision is made in clear peripheral cornea, at right angles to the first incision.
4. A continuous capsulorhexis is performed (Fig. 8.28a).
5. Hydrodissection is performed to mobilize the nucleus (Fig. 8.28b). A retrocortical 'fluid wave' over the red reflex can be observed, indicating completeness of hydrodissection.
6. 'Sculpting' of the nucleus is performed with the phaco probe to create a groove. The nucleus is rotated with a second instrument introduced through the second incision and a second groove is made at right angles to the first (Fig. 8.28c).
7. The phaco probe and the second instrument engage opposite walls of the nuclear groove.
8. The nucleus is cracked in the base of the groove by applying force in opposite directions (Fig. 8.28d).
9. The nucleus is rotated 90° and a crack made in the perpendicular furrow in a similar manner.
10. Each quadrant of the nucleus is fragmented, emulsified and aspirated in turn (Fig. 8.28e).
11. The remaining cortex is aspirated (Fig. 8.28f).
12. Viscoelastic substance is injected to inflate the capsular bag.
13. The incision is enlarged, if necessary, and IOL inserted.
14. Viscoelastic substance is aspirated.
15. The wound is ideally self-healing and does not require suture.

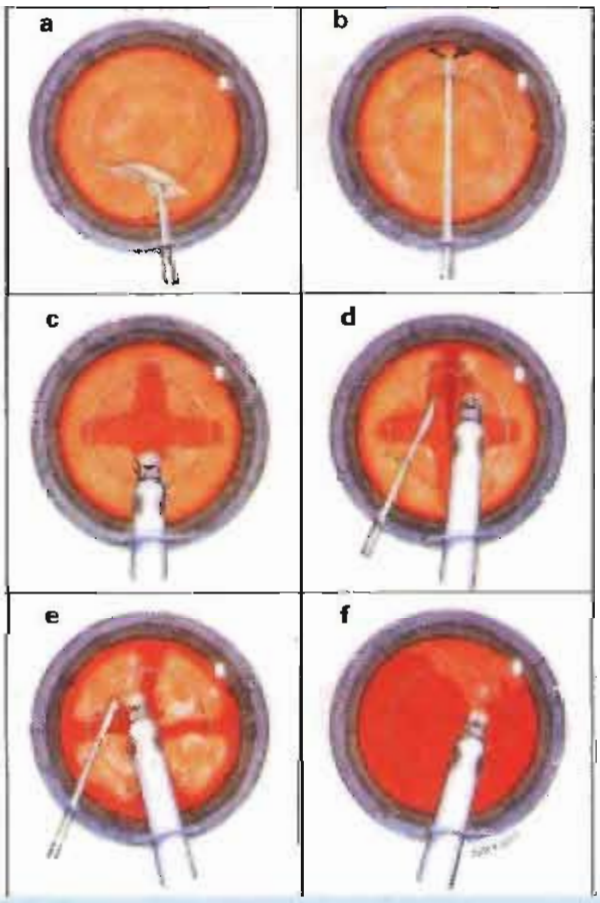

Fig. 8.28
Phacoemulsification (see *text*)

Operative complications

Rupture of the posterior capsule

This is potentially serious because it may be accompanied by vitreous loss, posterior migration of lens material and rarely expulsive haemorrhage. Long-term complications of vitreous loss, particularly if inappropriately managed, include uphitis, pupil, uveitis, vitreous touch, vitreous wick syndrome, secondary glaucoma, posterior dislocation of the IOL, retinal detachment and chronic cystoid macular oedema.

1. Signs
- Sudden deepening of the anterior chamber and momentary pupillary dilatation.
- The nucleus falls away and will not come towards the phaco tip.
- Vitreous may be aspirated into the phaco tip.
- The torn capsule or vitreous may be directly visible.

2. Management depends on the point in the procedure at which the tear occurred, the magnitude of the tear and the presence or absence of vitreous prolapse. The main principles of management are as follows:

a. Viscoelastic substance may be injected behind nuclear material with the purpose of expressing it into the anterior chamber and also preventing anterior herniation of vitreous.
b. A lens glide is passed behind the lens fragments to cover the capsular defect.
c. The lens fragments are expressed by visco-expression or removed by phaco.
d. All vitreous must be removed from the anterior chamber and the wound with a vitrector.
e. A decision has to be taken whether or not to implant an IOL based on the following criteria:

- If there is significant loss of lens material into the vitreous cavity, an IOL should not be implanted, since it may compromise visualization of the fundus, vital to successful pars plana vitrectomy (*see* later). IOL implantation can be performed at the time of vitrectomy.
- A very small posterior capsular tear may allow careful in-the-bag implantation of a PC-IOL.
- A large tear may still allow ciliary sulcus fixation of a PC-IOL with the optic captured in the capsular bag, especially if the anterior capsulorhexis is intact.
- Insufficient capsular support may necessitate that the IOL be sutured to the sulcus or alternatively, that an AC-IOL be implanted with the aid of a glide (Fig. 8.29). AC-IOLs are, however, associated with a higher risk of complications including bullous keratopathy, hyphaema, iris tuck and pupillary irregularities.

NB: Conditions may not be favourable for correct positioning even of an AC-IOL. It may then be safer not to proceed with lens implantation and to consider visual rehabilitation with a contact lens or secondary IOL implantation at a later date.

Posterior loss of lens fragments

Dislocation of fragments of lens material into the vitreous cavity (Fig. 8.30) after zonular dehiscence or posterior capsule rupture is rare but potentially serious because it may result in glaucoma, chronic uveitis, retinal detachment and chronic cystoid macular oedema. This complication is more commonly associated with phaco than ECCE. Initially, any uveitis or raised intraocular pressure must be treated. The patient should then be referred to a vitreoretinal surgeon for removal of nuclear fragments by pars plana vitrectomy.

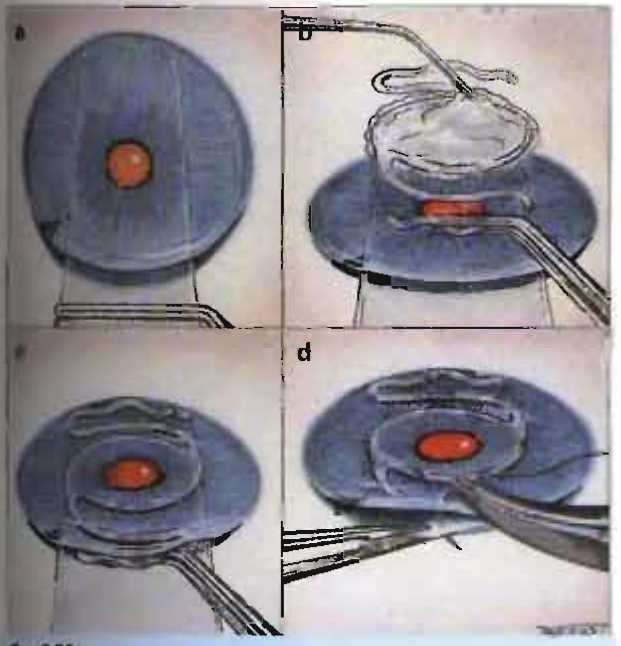

Fig. 8.29
Insertion of an anterior chamber intraocular lens

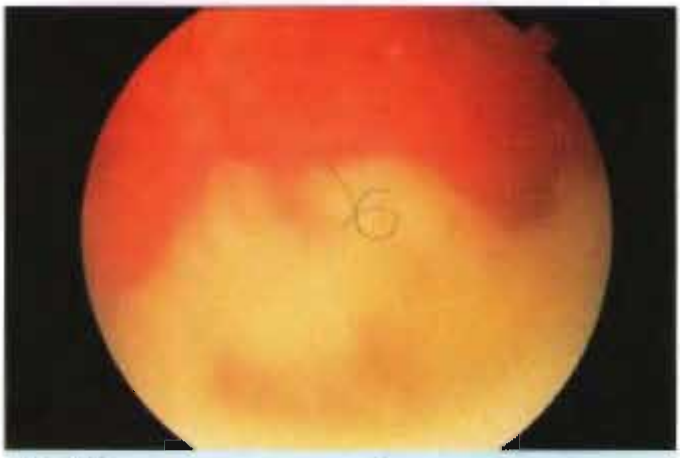

Fig. 8.30
Nuclear material in the vitreous

1. **Timing of surgery** is controversial. Some suggest the fragments be removed within the first week as later removal is associated with poorer visual outcome. Others recommend that surgery should be deferred for 2–3 weeks provided uveitis and raised intraocular pressure are controlled medically. This allows the lens material to become hydrated and softer, facilitating removal with a vitreous cutter alone (*see* below).
2. **Surgical technique** involves pars plana vitrectomy and removal of soft fragments with a vitreous cutter. Hard nuclear fragments are floated clear of the retina with heavy liquids (i.e. perfluorocarbons) and either emulsified with the fragmatome in the mid-vitreous cavity or delivered via a corneal incision or scleral pocket. An alternative method of removing hard nuclear material involves crushing them between the illumination probe and the vitreous cutter and then 'force feeding' them into the cutting port.

Posterior dislocation of IOL

Dislocation of a PC-IOL into the vitreous cavity reflects inappropriate implantation and is rare but serious. If the IOL is left it may lead to vitreous haemorrhage, retinal detachment, uveitis and chronic cystoid macular oedema. Treatment involves pars plana vitrectomy with removal, repositioning or exchange of the IOL. If adequate capsular support is present the same IOL may be repositioned into the ciliary sulcus. Inadequate capsular support affords the following alternatives: (a) removing the IOL and leaving the eye aphakic, (b) removing the IOL and replacing it with an AC-IOL, (c) scleral fixation of the existing IOL with a non-absorbable suture and (d) using an iris-fixated IOL.

Suprachoroidal haemorrhage

This is a bleed into the suprachoroidal space which may result in extrusion of intraocular contents (expulsive haemorrhage) or apposition of retinal surfaces. It is a dreaded but rare complication and much less likely with phaco-

emulsification. The source of the bleeding is a ruptured long or short posterior ciliary artery. Although the exact cause is unknown, contributing factors include advanced age, glaucoma, increased axial length, systemic cardiovascular disease and vitreous loss.

1. **Signs** (in chronological order)
   - Progressive shallowing of the anterior chamber, increased intraocular pressure and prolapse of the iris.
   - Vitreous extrusion, loss of the red reflex and the appearance of a dark mound behind the pupil.
   - In severe cases, all intraocular contents may be extruded through the incision.
2. **Immediate treatment** involves closure of the incision. Although posterior sclerotomy has been advocated, it may actually exacerbate the bleeding and result in a vicious circle with loss of the eye. Postoperatively, the patient should be treated with topical and systemic steroids to reduce intraocular inflammation.
3. **Subsequent management**
   a. Ultrasonography may be used to assess severity (Fig. 8.31).
   b. Surgery is performed 7–14 days later when the blood clot has liquefied. The blood is drained, and pars plana vitrectomy with air–fluid exchange performed (Fig. 8.32). Although the visual prognosis is grave, useful vision may be salvaged in some cases.

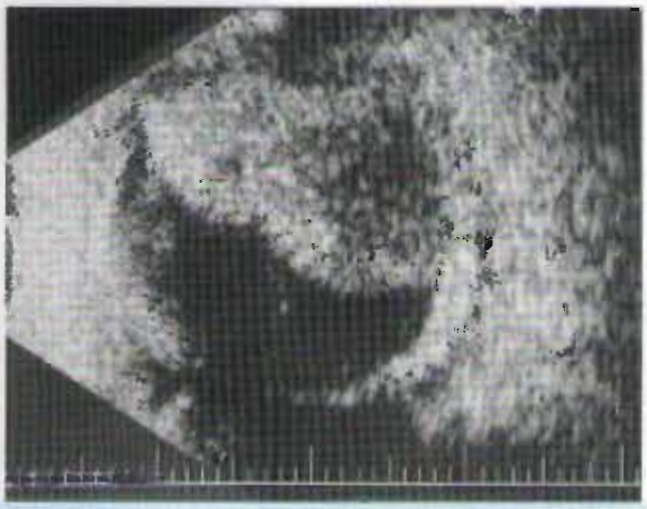

Fig. 8.31
Ultrasonogram showing a large suprachoroidal haemorrhage

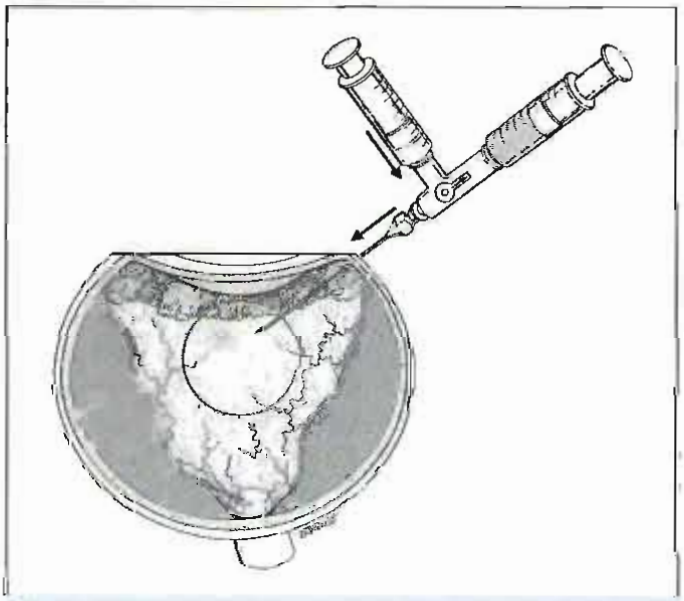

Fig. 8.32
Air–fluid exchange following vitrectomy for expulsive haemorrhage

Acute postoperative endophthalmitis

Causes

Acute endophthalmitis is a devastating complication that occurs in about 1:1000 cases.

1. **Causative organisms**, in order of frequency, include coagulase-negative staphylococci (e.g. *Staph. epidermidis*), other Gram-positive organisms (e.g. *Staph. aureus*) and Gram-negative organisms (e.g. *Pseudomonas* sp., *Proteus* sp.).
2. **The source of infection** most often cannot be identified with certainty. It is thought that the patient's own external bacterial flora of the eyelids, conjunctiva and lacrimal drainage passages is the most frequent culprit. Other potential sources of infection include contaminated solutions and instruments, and environmental flora including that of the surgeon and operating room personnel.

Prevention

Despite numerous studies, optimum prophylaxis has not yet been determined. The following measures may be beneficial:

1. **Preoperative treatment** of pre-existing infections such as staphylococcal blepharitis, conjunctivitis, dacryocystitis and infected contralateral sockets in patients with ocular prostheses (Fig. 8.33).
2. **Povidone–iodine** instilled preoperatively as follows:
   a. A 5% solution is prepared by diluting commercially available 10% Betadine aqueous solution used for skin

Fig. 8.33
Infected left socket of an artificial eye

preparation with an equal volume of balanced salt solution.

b. Two drops of the diluted solution are instilled into the conjunctival sac several minutes prior to surgery (Fig. 8.34) and the eyelids gently manipulated to distribute the solution over the ocular surface. The solution is also used to paint the skin of the eyelids, prior to draping (Fig. 8.35).

c. Prior to commencing surgery, the eye is irrigated with saline solution.

3. **Meticulous draping technique** that ensures that the lashes and lid margins are isolated (Fig. 8.36).
4. **Prophylactic antibiotics**
   - *a. Postoperative injection* of anterior sub-Tenon antibiotics is commonly performed, but evidence of its efficacy is scant.
   - *b. Intraoperative irrigation* of the anterior chamber by adding antibiotics such as vancomycin into the infusion fluid may be efficacious but may also lead to the emergence of resistant strains of bacteria.

Fig. 8.34
Preoperative instillation of povidone–iodine

Clinical features

The severity of endophthalmitis reflects the virulence of the offending organism.

1. **Extremely** severe endophthalmitis is characterized by pain, marked visual loss, lid oedema, chemosis,

Fig. 8.35
Preparation of the skin with povidone–iodine

Fig. 8.37
Large hypopyon in acute postoperative endophthalmitis

Fig. 8.36
Drapes isolating the eyelids from the operating field

Fig. 8.38
Fibrinous exudate and small hypopyon in acute postoperative endophthalmitis

conjunctival injection, purulent discharge, corneal infiltrates and a large hypopyon (Fig. 8.37).

2. **Moderately** severe endophthalmitis is characterized by fibrinous exudate in the anterior chamber, a smaller hypopyon (Fig. 8.38), vitritis, absent red reflex and inability to visualize the fundus even with the indirect ophthalmoscope (Fig. 8.39).
3. **Mild** endophthalmitis may be associated with only slight pain, absent or small hypopyon (Fig. 8.40) and preservation of some red reflex with abiltty to visualize some fundus details with the indirect ophthalmoscope.

NB: The time interval between surgery and onset of symptoms may be useful in predicting the likely offending organisms. For example:

- *Staph. aureus* and Gram-negative bacilli typically present 2–4 days postoperatively with florid endophthalmitis.
- *Staph. epidermidis* and coagulase-negative cocci usually present 5–7 days postoperatively with relatively milder signs.

Differential diagnosis

1. **Retained lens material** in the anterior chamber (Fig. 8.41) or vitreous may be associated with a severe anterior uveitis.
2. **Toxic reaction** to irrigating fluid or foreign material introduced into the eye at the time of surgery may occur. Rarely, an intense fibrinous reaction may develop on the anterior surface of the IOL (Fig. 8.42). Intensive topical and periocular steroids combined with cycloplegics are effective, although synechiae to the IOL may develop.
3. **Difficult or prolonged surgery** may result in corneal oedema and uveitis. This however, is evident in the immediate postoperative period.

Management

1. **Identification of causative organisms** from aqueous and vitreous confirms the diagnosis. However, negative culture does not necessarily rule out infection. The samples should be taken in the operating room as follows:

Fig. 8.39
Vitreous haze in acute postoperative endophthalmitis

Fig. 8.41
Retained lens material in the anterior chamber

Fig. 8.40
Small hypopyon in acute postoperative endophthalmitis

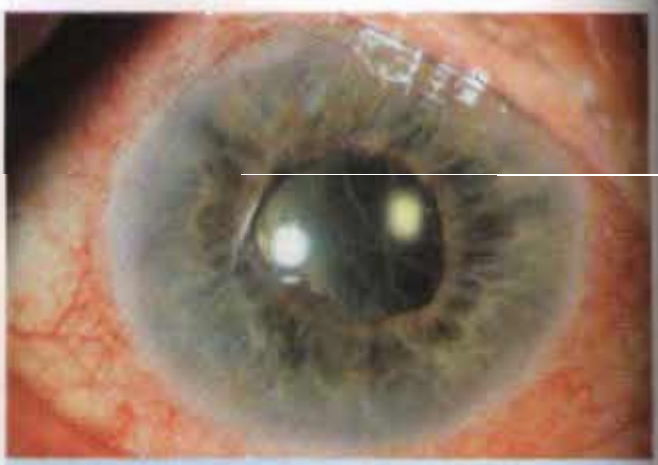

Fig. 8.42
Sterile fibrinous reaction following cataract extraction

a. ***Aqueous samples*** are obtained by aspirating 0.1 ml of aqueous with a needle on a tuberculin syringe, through the pre-existing 'second incision'.

b. ***Vitreous samples*** are ideally obtained with a mini-vitrector (Fig. 8.43) through a 'pars plana' sclerotomy 3.5 mm behind the limbus (Figs 8.44 and 8.45). If a mini-vitrector is unavailable, an alternative method involves a partial-thickness sclerotomy 3.5 mm behind the limbus, with aspiration of liquid vitreous from the mid-vitreous cavity with a needle attached to a tuberculin syringe. Between 0.1 and 0.3 ml of vitreous is removed and inoculated onto blood agar, chocolate agar, liquid thioglycolate and Sabouraud agar. If these culture media are not readily available, direct inoculation of blood culture bottles is a good alternative. Several drops are also placed onto slides for Gram and Giemsa staining.

Fig. 8.45
Mini-vitrector obtaining vitreous samples

Fig. 8.43
Mini-vitrector for obtaining vitreous samples

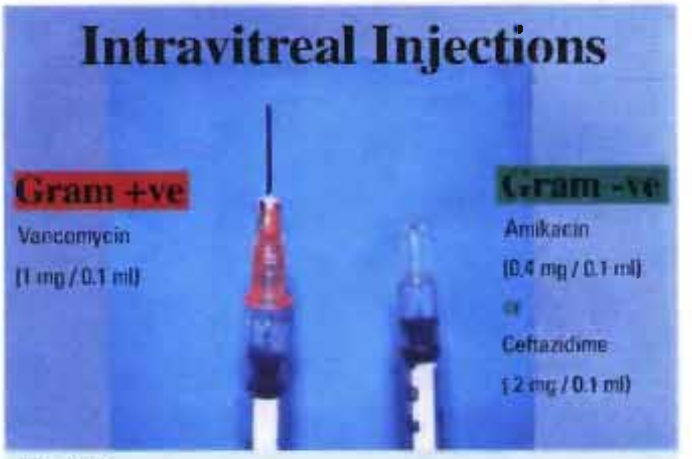

Fig. 8.46
Syringes containing antibiotics for intravitreal injection

Fig. 8.44
Calipers measuring 3.5 mm from the limbus

2. **Vitrectomy** is beneficial only in the context of severe infection with visual acuity reduced to 'light perception'. If visual acuity is 'hand movements' or better then vitrectomy is unnecessary.
3. **Antibiotics** used are amikacin or ceftazidime, to cover most Gram-positive and Gram-negative organisms, and vancomycin for coagulase-negative and coagulase-positive cocci (Fig. 8.46). Amikacin acts synergistically with vancomycin but is potentially more retinotoxic than ceftazidime, which is however, not synergistic with vancomycin.
   a. ***Intravitreal*** antibiotics should be administered immediately after culture specimens have been obtained and the eye has been softened. Amikacin (0.4 mg in 0.1 ml) or ceftazidime (2.0 mg in 0.1 ml) and vancomycin (1 mg in 0.1 ml) are injected slowly into the mid-vitreous cavity using a 25-gauge needle (Fig. 8.47). The bevel of the needle should face anteriorly so as to minimize contact between the drug and the macula. After the first injection has been given, the syringe is disconnected but the needle is left inside the vitreous cavity so that the second injection can be given through the same needle. If

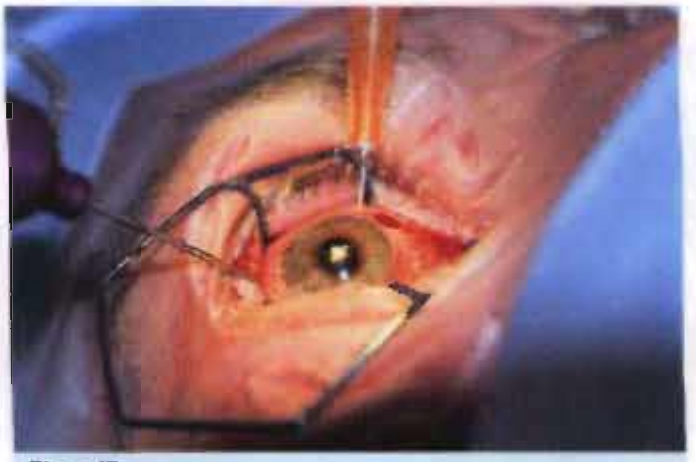

Fig. 8.47
Intravitreal injection of antibiotics

Fig. 8.48
Contraction of exudate following successful treatment

there is concern about the possibility of the formation of precipitates then two separate needles, each with a different antibiotic, may be used. The needle is then removed and a periocular injection of antibiotic given.

b. ***Periocular*** injections of vancomycin 25 mg and ceftazidime 100 mg, or gentamicin 20 mg and cefuroxime 125 mg, result in therapeutic intraocular concentrations and should be used. The injections are repeated daily for 5–7 days according to the response to therapy.

c. ***Topical*** therapy is of limited benefit in the absence of associated infectious keratitis.

d. ***Systemic*** therapy is controversial. The Endophthalmitis Vitrectomy Study Group showed that systemic ceftazidime and amikacin were not beneficial. These water-soluble antibiotics also have relatively poor coverage for Gram-positive organisms and poor ocular penetration. It is therefore possible that other antibiotics, such as the lipid-soluble quinolones (e.g. ciprofloxacin, ofloxacin) and imipenem, which have better penetration and a larger antimicrobial spectrum, may be beneficial. This can only be answered by future studies.

4. **Steroid** therapy should be commenced after antibiotics have been administered to limit the amount of inflammatory-induced damage. Steroids will not interfere with the control of the infection, provided the organisms are sensitive to the antibiotics.
   a. ***Periocular*** betamethasone 4 mg or dexamethasone 4 mg (1 ml) is administered daily for 5–7 days according to response to therapy.
   b. ***Oral*** prednisolone 20 mg q.i.d. for 10–14 days may be considered in very severe cases.
   c. ***Topical*** 0.1% dexamethasone is initially given every 30 minutes and then less frequently.
5. **Subsequent management** is to a certain extent governed by culture results and clinical findings.
   - Signs of improvement include reduction of anterior chamber cellular activity and hypopyon, and contraction of fibrinous exudate (Fig. 8.48). In this situation treatment is not modified irrespective of culture results.
   - If resistant bacteria are cultured and the clinical findings are worsening, antibiotic therapy should be modified accordingly. However, it is often too late.
6. **Results** of treatment are poor despite aggressive and appropriate therapy, with 55% of eyes achieving a final visual acuity of 6/60 or less.

> ***NB:*** In some cases poor vision may be caused by antibiotic retinotoxicity, particularly aminoglycosides. Figure 8.49 shows macular infarction following intravitreal antibiotic injection. Figure 8.49a shows pallor of the posterior pole with haemorrhages. The fluorescein angiogram (Figs 8.49b–d) shows hypofluorescence due to ischaemia.

Delayed chronic postoperative endophthalmitis

Delayed chronic indolent endophthalmitis occurs when an organism of low virulence becomes trapped within the capsular bag. It has an onset ranging from 4 weeks to years (mean of 9 months) postoperatively and typically follows uneventful cataract extraction with a PC-IOL. It may rarely be precipitated by YAG laser capsulotomy, which releases the sequestrated organisms from the posterior capsule into the vitreous. The infection is caused most frequently by *Propionibacterium acnes* and occasionally *Staph. epidermidis*, *Actinomyces israelii* and *Corynebacterium* spp.

Clinical features

1. **Presentation** is with mild progressive visual deterioration which may be associated with floaters but without pain.
2. **Signs**
   - Low-grade anterior uveitis, sometimes with granulomatous features such as mutton-fat keratic precipitates (Fig. 8.50).
   - Vitritis is common but hypopyon occurs infrequently.

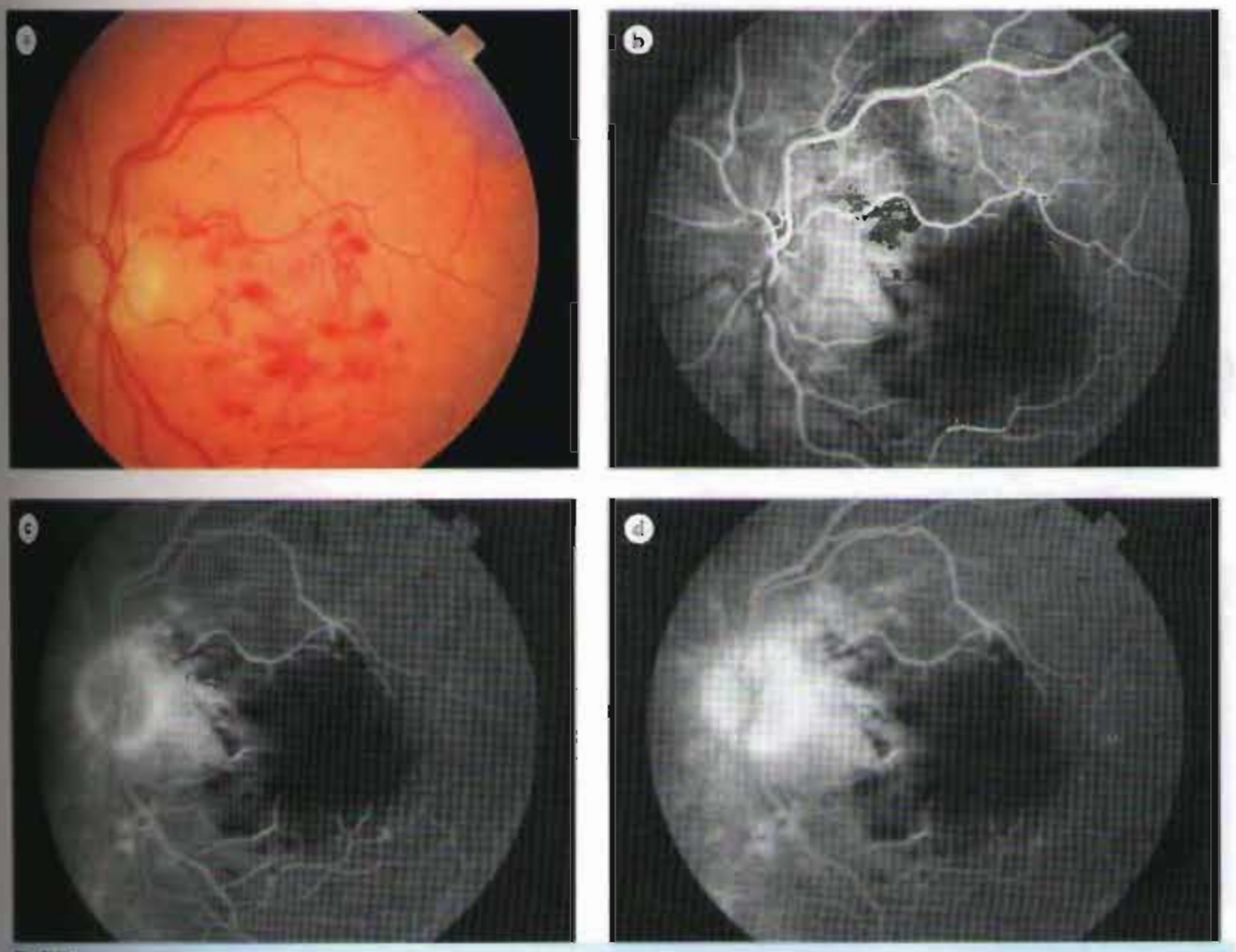

Fig. 8.49
Macular ischaemia following intravitreal antibiotic injection (see text)

Fig. 8.50
Mutton-fat keratic precipitates in chronic postoperative endophthalmitis

Fig. 8.51
White capsular plaque in chronic postoperative endophthalmitis

- An enlarging white capsular plaque is highly suggestive of infection by *Propionibacterium acnes*. It is composed of sequestered collections of organisms inside the peripheral capsular bag (Fig. 8.51).

NB: It is important to perform gonioscopy under mydriasis so as not to miss an equatorial plaque.

Fig. 8.52
Fewer keratic precipitates following topical steroid therapy in chronic postoperative endophthalmitis

Fig. 8.53
Severe recurrence of inflammation 2 weeks following cessation of steroid therapy

3. **Clinical course.** The inflammation initially responds well to topical steroids (Fig. 8.52), but recurs after cessation of treatment (Fig. 8.53) and then becomes refractory.

Investigations

The diagnosis should be confirmed by cultures of the aqueous and vitreous with growth of the organisms on thioglycolate broth. Unfortunately this frequently fails to show the causative organism, mainly because of the small number and low pathogenicity of the pathogens, which may take 10–14 days to grow. Detection of pathogens can be greatly improved with the polymerase chain reaction (PCR).

Treatment

This is difficult because the sequestered organisms are isolated from host defences and antibiotics.

1. Topical and periocular steroids, and antibiotics may be tried but the response is transient.
2. Intravitreal vancomycin (1 mg in 0.1 ml) alone or combined with pars plana vitrectomy is successful in 50%.
3. Removal of the capsular bag, residual cortex and IOL may eventually be required. Secondary IOL implantation may be considered at a later date.

Postoperative capsular opacification

Posterior capsular opacification

Visually significant posterior capsular opacification (PCO) is the most common late complication of uncomplicated cataract surgery. Apart from reducing visual acuity, PCO may impair contrast sensitivity, cause difficulties with glare or give rise to monocular diplopia. Certain acrylic IOLs may be associated with lower rates of PCO than PMMA and silicone lenses. Implant design may also be relevant in this context; notably, a square 'edge' to the optic appears to inhibit PCO.

1. **Clinical features**
   a. ***Elschnig pearls*** (bladder cells, Wedl cells) are caused by the proliferation and migration of residual equatorial epithelial cells along the posterior capsule at the site of apposition between the remnants of the anterior capsule and the posterior capsule. They impart a vacuolated appearance to the posterior capsule, best visualized on retroillumination (Fig. 8.54). This is the most frequently seen type of opacification and is related to the patient's age. It is extremely common in children if a posterior capsulorhexis is not performed at the time of surgery.
   b. ***Capsular fibrosis*** (Fig. 8.55), due to fibrous metaplasia of epithelial cells, is less common and usually appears earlier than Elschnig pearls.
2. **Treatment** involves the creation of an opening in the posterior capsule with the Nd:YAG laser. Indications for capsulotomy include:
   - Diminished visual acuity.
   - Diplopia or glare, secondary to capsular wrinkling.
   - Inadequate fundus view impairing diagnosis, monitoring or treatment of retinal pathology.

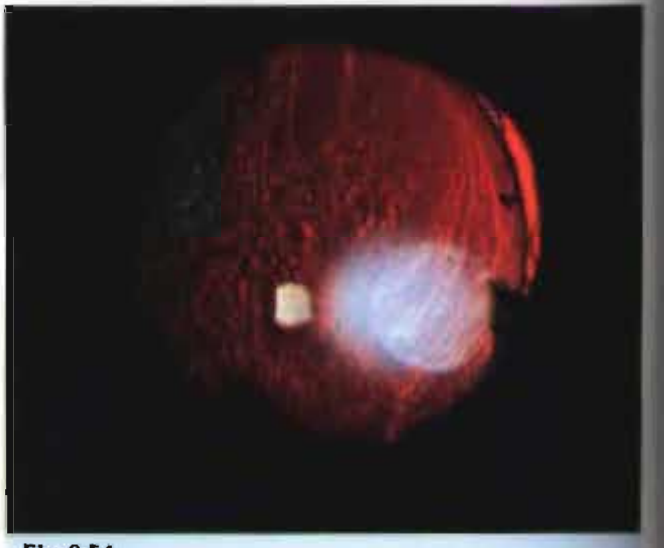

Fig. 8.54
Elschnig pearls

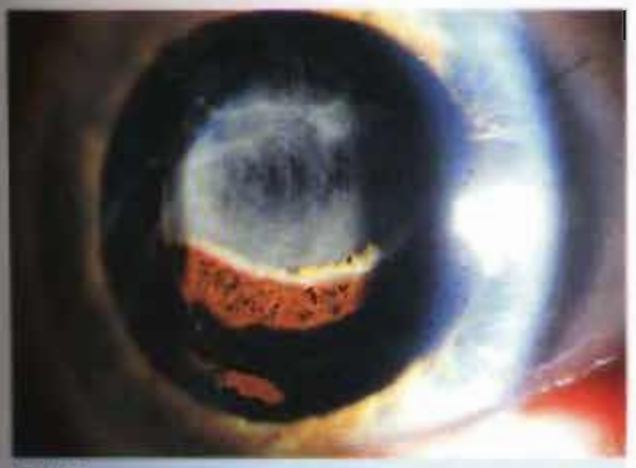

Fig. 8.55
Capsular fibrosis

Fig. 8.57
Laser pitting of the intraocular implant

1. **Technique.** Safe and successful laser capsulotomy involves accurate focusing and using the minimum energy required. Laser power is initially set at 1 mJ/pulse, and may be increased if necessary. A series of punctures are applied in a cruciate pattern, the first puncture aimed at the visual axis (Fig. 8.56). An opening of about 3 mm is usually adequate, but larger capsulotomies may be necessary for retinal examination or photocoagulation.
4. **Complications**
   a. *Damage to the IOL* ('pitting') (Fig. 8.57) may occur if the laser is poorly focused. Although undesirable, a few laser marks on the IOL do not alter visual function or impair ocular tolerance of the IOL.
   b. *Cystoid macular oedema* is an occasional complication and may develop months after capsulotomy. It is less common when capsulotomy is delayed for 6 months or more after cataract surgery.
   c. ***Rhegmatogenous retinal detachment*** is rare, except in high myopes, and may occur several months after capsulotomy.
   d. ***Intraocular pressure elevation***, which is mild and transient, is usually innocuous. However, sustained elevation above precapsulotomy levels may occur, especially in patients with established glaucoma or those that manifest significant ocular hypertension within hours of the capsulotomy.
   e. ***Posterior IOL subluxation or dislocation*** (Fig. 8.58) is rare but may occur, particularly with plate haptic silicone and hydrogel IOLs.
   f. ***Chronic endophthalmitis*** due to release of sequestered organisms into the vitreous is very rare (*see* above).

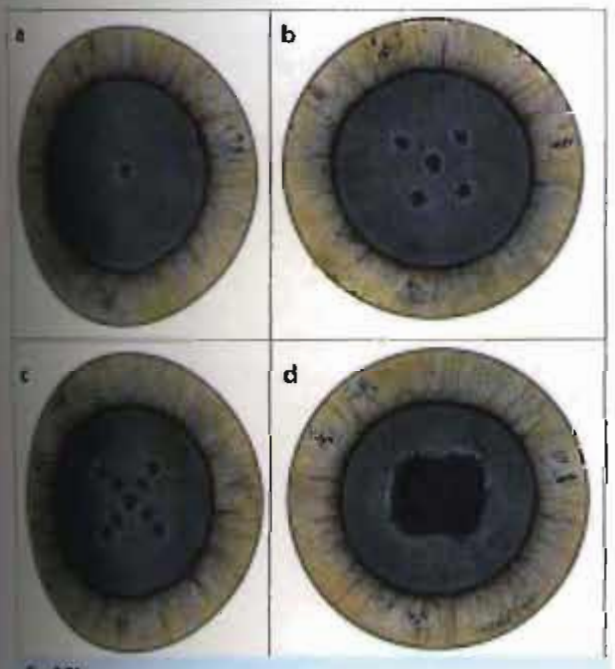

Fig. 8.56
Technique of Nd:YAG laser posterior capsulotomy

NB: Most patients who develop complications have no identifiable risk factor. The number of laser pulses and the energy level are probably not related to their development.

Fig. 8.58
Dislocation of an intraocular implant

Fig. 8.59
Anterior capsular opacification and capsulophimosis

Anterior capsular opacification

Anterior capsular opacification (ACO), also called anterior capsular fibrosis or anterior subcapsular opacification, is less common but occurs earlier than PCO, sometimes within 1 month postoperatively. Severe fibrosis may result in anterior capsular shrinkage and constriction of the capsulorhexis (capsulophimosis) (Fig. 8.59). IOL design and material may be relevant in the development of ACO. The highest rate is with plate-haptic silicone IOLs and the lowest with three-piece acrylic optic–PMMA haptic IOLs. A small capsulorhexis may also be of relevance.

Miscellaneous postoperative complications

Corneal oedema

Corneal oedema (*see* Fig. 5.9) is usually transient and often caused by intraoperative trauma to the endothelium by contact with lens matter, instruments or IOL. Eyes with pre-existing Fuchs endothelial dystrophy are at increased risk. Other causes include excessive power use during phaco-emulsification, complicated or prolonged surgery, and postoperative ocular hypertension.

Iris prolapse

Iris prolapse is extremely rare following small incision surgery but may occur after ECCE (Fig. 8.60).

1. **Causes**
   - A phaco incision with a peripheral point of entry into the anterior chamber.
   - A leaking incision.
   - Inadequate suturing of an ECCE incision.
   - Patient-related factors such as coughing and straining.
2. **Clinical features**
   - Prolapsed uveal tissue may be visible on the ocular surface.
   - The anterior chamber may be shallow in the area of the incision.
   - The pupil may be peaked (drawn) towards the prolapse.
3. **Complications** include defective wound healing, excessive astigmatism, epithelial ingrowth, chronic anterior uveitis, cystoid macular oedema and endophthalmitis.
4. **Treatment** depends on the time interval between cataract surgery and identification of the prolapse. If discovered within a day or two, with no evidence of infection, the prolapsed iris may be reposited and the incision resutured. If, however, the prolapse is of longer duration, the risk of infection mandates that the prolapsed iris be excised.

Malposition of IOL

Although uncommon, malposition may be associated with both optical and structural problems. Annoying visual aberrations include glare, haloes, and monocular diplopia if the edge of the IOL becomes displaced into the pupil (Fig. 8.61).

1. **Causes**
   - Primary malposition occurs during initial surgery. This may be due to zonulodialysis, capsular rupture, or after

Fig. 8.60
Iris prolapse

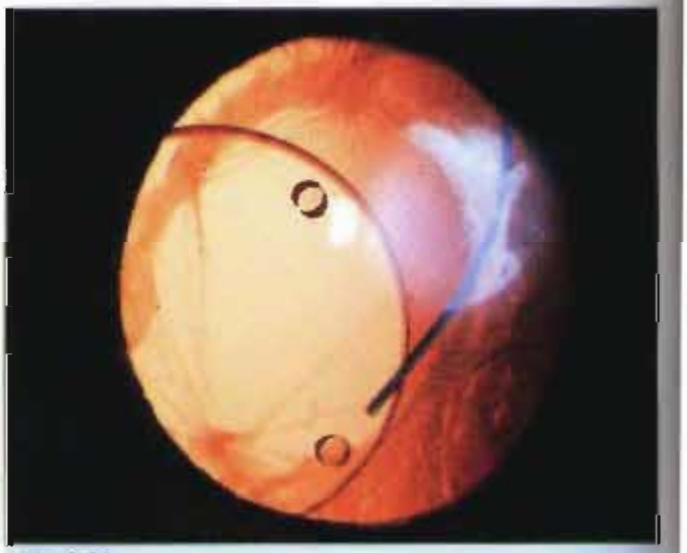

Fig. 8.61
Decentration of an intraocular implant

routine phacoemulsification, when one haptic is inserted into the capsular bag and the other into the ciliary sulcus.
- Postoperative causes include trauma, eye rubbing and capsular contraction.

2. **Treatment** with miotics may be successful in mild cases. Significant malposition may necessitate replacement of the IOL.

Retinal detachment

Rhegmatogenous retinal detachment, although uncommon following uneventful ECCE or phaco, may be associated with the following risk factors:

1. **Preoperative**
   - Lattice degeneration or retinal breaks should be treated prophylactically prior to cataract surgery or laser capsulotomy if fundus view permits, or as soon as possible thereafter.
   - High myopia.
2. **Operative**
   - Disruption of the posterior capsule.
   - Vitreous loss, particularly if managed inappropriately, is associated with an approximate 7% risk of retinal detachment. Myopia of over 6D increases the risk to 15%.
3. **Postoperative**. YAG laser capsulotomy, if performed within a year of cataract surgery.

Cystoid macular oedema

This occurs commonly after complicated surgery involving rupture of the posterior capsule and vitreous prolapse, sometimes with incarceration in the incision, although it may occur after uneventful surgery. It usually presents 2–6 months after surgery. The clinical features and management are discussed in Chapter 13.

Congenital cataract

Congenital cataracts occur in about 3:10,000 live births; two-thirds of cases are bilateral. The cause of cataract formation can be identified in about half of those with bilateral opacities. The most common cause is genetic mutation, usually AD. Other causes include chromosomal abnormalities such as Down syndrome, metabolic disorders such as galactosaemia and intrauterine insults such as rubella infection. Congenital cataract may also occur as part of a complex developmental disorder of the eye such as aniridia.

Cataract without systemic associations

Isolated hereditary cataracts

These account for about 25% of cases. The mode of inheritance is most frequently AD but may be autosomal recessive (AR) or X-linked (X-L). The morphology of the opacities and also frequently the need for surgery are usually similar in parent and offspring. About 10 loci for AD cataract have been mapped. Isolated inherited congenital cataracts carry a better visual prognosis than those with coexisting ocular and systemic abnormalities. This is because they are frequently partial at birth so that surgery may be delayed until the child is older, when there is a lower incidence of surgical complications and refractive correction is easier. Morphological classification of hereditary cataracts is based on the location of the opacities within the lens as follows:

1. **Zonular cataract** in which the opacity occupies a discrete zone in the lens may be:
   a. Nuclear, in which the opacities are confined to the embryonic or fetal nuclei of the lens. Some patients have dense central opacities (Fig. 8.62) while others have fine pulverulent (dust-like) opacities (Fig. 8.63).
   b. Lamellar, in which the opacity is sandwiched between clear nucleus and cortex. It may be associated with radial extensions known as riders (Fig. 8.64).
   c. Capsular, in which the opacity is confined to the anterior or posterior capsule.

Fig. 8.62
Congenital nuclear cataract

Fig. 8.63
Congenital nuclear pulverulent cataract

Fig. 8.64
Congenital lamellar cataract

Fig. 8.67
Congenital anterior pyramidal cataract (Courtesy of A. Shun-Shin)

Fig. 8.65
Congenital sutural cataract

Fig. 8.68
Congenital anterior polar cataract and persistent pupillary membrane

Fig. 8.66
Congenital flat anterior polar cataract

Fig. 8.69
Congenital posterior polar cataract

d. ***Sutural***, in which the opacity follows the anterior or posterior Y suture. It may occur in isolation or in association with other opacities (Fig. 8.65).

2. **Polar cataract**, in which the opacities occupy the subcapsular cortex at the anterior or posterior pole of the lens.

a. ***Anterior*** polar cataract may be flat (Fig. 8.66) or project as a conical opacity into the anterior chamber (pyramidal cataract) (Fig. 8.67). Patients with pyramidal cataracts are likely to develop amblyopia due to either unilateral involvement or bilateral asymmetrical opacities. Occasional association of

anterior polar cataracts include persistent pupillary membrane (Fig. 8.68), anterior lenticonus, Peters anomaly and aniridia.

b. *Posterior* polar cataract (Fig. 8.69) may occasionally be associated with persistent hyaloid remnants (Mittendorf dots), posterior lenticonus and persistent hyperplastic primary vitreous.

Other types

1. **Coronary (supranuclear)** cataract consists of round opacities in the deep cortex which surround the nucleus like a crown (Fig. 8.70). They are usually sporadic and only occasionally hereditary.
2. **Blue dot** opacities (cataracta punctata caerulea) (Fig. 8.71) are common and innocuous and may coexist with other types of lens opacities.
3. **Total** (mature) cataracts are frequently bilateral and often begin as lamellar or nuclear.
4. **Membranous** cataract (Fig. 8.72) is rare and may be associated with Hallermann–Streiff–Francois syndrome. It occurs when lenticular material partially or completely reabsorbs, leaving behind residual chalky-white lens matter sandwiched between the anterior and posterior capsules.

Fig. 8.70
Congenital coronary (supranuclear) cataracts

Fig. 8.71
Congenital blue dot cataract

Fig. 8.72
Congenital membranous cataract

Systemic associations

A great many systemic paediatric conditions may be associated with congenital cataracts. The vast majority are extremely rare and of interest only to paediatric ophthalmologists. The general ophthalmologist should, however, be aware of the following conditions:

Metabolic

1. **Galactosaemia** involves severe impairment of galactose utilization caused by absence of the enzyme galactose-1-phosphate uridyl transferase (GPUT). Inheritance is AR.
   a. ***Systemic features***, which become manifest during infancy, include failure to thrive, lethargy, vomiting and diarrhoea. Reducing substance is found in the urine after drinking milk. Unless galactose, in the form of milk and milk products, is withheld from the diet, hepatosplenomegaly, renal disease, anaemia, deafness and mental handicap occur subsequently, with ultimate death.
   b. ***Cataract***, characterized by a central 'oil droplet' opacity (Fig. 8.73), develops within the first few days or weeks

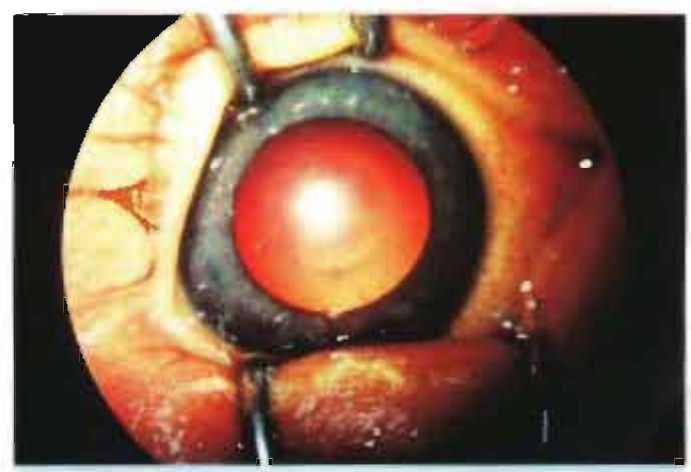

Fig. 8.73
'Oil droplet' cataract in galactosaemia (Courtesy of K. Nischal)

of life in a large percentage of patients. The exclusion of galactose (in milk products) from the diet will prevent the progression of cataract and may reverse early lens changes.

2. **Galactokinase deficiency** involves the first enzyme in the pathway of galactose metabolism. Inheritance is AR.
   a. ***Systemic features*** are absent although reducing substance is present in the urine after drinking milk.
   b. ***Cataract***, consisting of lamellar opacities, may develop in the fetus or in early infancy. Some presenile cataracts may also result from galactokinase deficiency. Galactose is only indirectly cataractogenic as a result of its reduction to dulcitol within the lens. Dulcitol accumulation within the lens increases the intralenticular osmotic pressure with resultant osmotic influx of water, disruption of the lens fibres and opacification.
3. **Lowe (oculocerebrorenal) syndrome** is a rare inborn error of amino acid metabolism which predominantly affects boys. Inheritance is X-L.
   a. ***Systemic features*** include mental handicap, Fanconi syndrome of the proximal renal tubules, muscular hypotonia, frontal prominence and sunken eyes. It is one of the few conditions in which congenital cataract and congenital glaucoma may coexist.
   b. ***Cataract*** is universal; the lens is also small, thin and disc-like (microphakia) and may show posterior lentiglobus. Cataract may be capsular, lamellar, nuclear or total. Female carriers manifest micropunctate cortical lens opacities usually without visual impact.
   c. ***Congenital glaucoma*** is present in 50% of cases.
4. **Other** disorders include hypoparathyroidism, pseudohypoparathyroidism and mannosidosis.

Prenatal infections

1. **Congenital rubella** is associated with cataract in about 15% of cases. After the gestational age of 6 weeks, the virus is incapable of crossing the lens capsule so that the lens is immune. Although the lens opacities (which may be unilateral or bilateral) are usually present at birth, they may occasionally develop several weeks or even months later. The opacity may involve the nucleus, with a dense pearly appearance, or may present as a more diffuse opacity involving most of the lens. The virus is capable of persisting within the lens for up to 3 years after birth.
2. **Other** intrauterine infections that may be associated with neonatal cataract are toxoplasmosis, cytomegalovirus, herpes simplex and varicella.

Chromosomal abnormalities

1. **Down syndrome** (trisomy 21)
   a. ***Systemic features*** include mental handicap, upward-slanting palpebral fissures, epicanthic folds, flat midface with relative prognathism, brachycephalic skull with flattening of the occiput, broad and short hands and a protruding tongue.
   b. ***Cataract*** of various morphology occurs in about 5% of patients. The opacities are usually symmetrical and often develop late in childhood.
2. **Other** chromosomal abnormalities associated with cataract include Patau (trisomy 13) and Edward (trisomy 18) syndromes.

Skeletal syndromes

1. **Hallermann–Streiff–Francois syndrome** is a sporadic disorder.
   a. ***Systemic features*** include frontal prominence, small beaked nose, baldness, progeria, micrognathia and pointed chin, short stature and hypodontia.
   b. ***Cataract***, which may be membranous (*see* Figure 8.7), occurs in 90% of cases.
2. **Nance–Horan syndrome** is an X-L disorder.
   a. ***Systemic features*** include supernumerary incisors, prominent ears, anteverted pinnae and shortened metacarpals.
   b. ***Cataract*** may be dense and associated with mild microphthalmos. Female carriers may show mild sutural lens opacities.

Management

Ocular examination

Since a formal estimate of visual acuity cannot be obtained in the neonate, reliance is required on the density and morphology of the opacity, other ocular associated findings and visual behaviour of the child, in order to assess the visual significance of the cataract.

1. **Density** and potential impact on visual function are assessed on the basis of appearance of the red reflex and the quality of the fundus view on direct and indirect ophthalmoscopy. However, slit-lamp examination of a neonate has been made easier with the introduction of high-quality portable slit-lamps. With assistance to restrain head movements, detailed anterior segment assessment should be possible. On ophthalmoscopy cataract density is graded as follows:
   - A very dense cataract occluding the pupil will preclude any view with either instrument and the decision to operate is straightforward.
   - A less dense cataract, which is, however, still visually significant, will allow visualization of the retinal vasculature with the indirect but not with the direct ophthalmoscope. Other features of visually significant cataract are central or posterior opacities over 3 mm in diameter.
   - A visually insignificant opacity will allow clear visualization of the retinal vasculature with both the indirect and direct ophthalmoscope. Other features of visually insignificant cataract are central opacities less than 3 mm in diameter and peripheral, anterior or punctate opacities with intervening clear zones.

2. **Morphology** of the opacity can give important clues to aetiology, as described previously.
3. **Associated ocular pathology** may involve the anterior segment (corneal clouding, microphthalmos, glaucoma, persistent hyperplastic primary vitreous) or the posterior segment (chorioretinitis, Leber amaurosis, rubella retinopathy, foveal or optic nerve hypoplasia). Examination under general anaesthesia may occasionally be required, as may repeated examinations, to document progression of cataract or associated disease.
4. **Other indicators** of severe visual impairment include absence of central fixation, nystagmus and strabismus. Nystagmus in particular signifies a poor visual prognosis.
5. **Special tests** such as forced choice preferential looking (see Chapter 16) and visually evoked potentials also provide helpful information but should not be relied upon exclusively since they may be misleading.

Systemic investigations

Unless there is an established hereditary basis for the cataracts, the investigation of the infant with bilateral cataracts should include the following:

1. **Serological tests** for intrauterine infections (TORCH = **t**oxoplasmosis, **r**ubella, **c**ytomegalovirus and **h**erpes simplex). A history of maternal rash during pregnancy mandates the assay of varicella zoster antibody titres.
2. **Urine**. Urinalysis for reducing substance after drinking milk (galactosaemia) and chromatography for amino acids (Lowe syndrome).
3. **Other investigations** include fasting blood glucose, serum calcium and phosphorus, red blood cell GPUT and galactokinase levels.
4. **Referral to a paediatrician** may be warranted for dysmorphic features or suspicion of other systemic diseases. Chromosome analysis may be useful in this context.

Timing of surgery

This is crucial and the main considerations are as follows:

1. **Bilateral dense** cataracts (Fig. 8.74) require early surgery (i.e. by 6 weeks of age) to prevent the development of stimulus deprivation amblyopia. If the severity is asymmetrical, the eye with the denser cataract should be addressed first.

Fig. 8.74
Bilateral dense congenital cataracts

2. **Bilateral partial** cataracts may not require surgery until later, if at all. In cases of doubt it may be prudent to defer surgery, monitor lens opacities and visual function and intervene later if vision deteriorates.
3. **Unilateral dense** cataracts merit urgent surgery (within days) followed by aggressive anti-amblyopia therapy, despite which the results are often poor. If the cataract is detected after 16 weeks of age then surgery is inadvisable because amblyopia is refractory.
4. **Partial unilateral** cataracts can usually be observed or treated non-surgically with pupillary dilatation and possibly part-time contralateral occlusion to prevent amblyopia.

> ***NB:*** It is important to correct associated refractive errors.

Surgical technique

1. A 'scleral tunnel', 6 mm in width, is fashioned.
2. The anterior chamber is entered with a keratome (usually 3 mm wide) and the anterior chamber filled with viscoelastic substance.
3. An anterior capsulorhexis is performed. In children the anterior capsule is more elastic than in adults and the rhexis may be difficult due to a tendency to run outwards.
4. The lens matter is aspirated with a vitreous cutter or a Simcoe cannula.
5. A capsulorhexis is then performed on the posterior capsule.
6. A limited anterior vitrectomy is performed with a vitrector.
7. A PMMA posterior chamber IOL is implanted into the capsular bag, if appropriate. Some surgeons prolapse the optic through the posterior capsulotomy.
8. The viscoelastic substance is aspirated.
9. Intraocular scissors and forceps may be required to excise thick capsular material or retrolenticular plaques in eyes with associated persistent hyperplastic primary vitreous. Intraocular bipolar cautery may also be necessary to seal bleeding vessels.
10. A well-constructed scleral tunnel often will not require a suture.

Postoperative complications

Cataract surgery in children carries a higher incidence of complications than in adults.

1. **Posterior capsular opacification** is nearly universal if the posterior capsule is retained. It is also of more significance in young children because of its amblyogenic effect. Opacification of the anterior hyaloid face may occur despite posterior capsulorhexis if the anterior vitreous is left intact. The incidence of opacification is reduced when posterior capsulorhexis is combined with vitrectomy.

Fig. 8.75
Soemmerring ring following congenital cataract surgery

2. **Secondary membranes** may form across the pupil, particularly in microphthalmic eyes or those with associated chronic uveitis. A fibrinous postoperative uveitis in an otherwise normal eye, unless vigorously treated, may also result in membrane formation. Thin membranes may be opened with an Nd:YAG laser; thick ones may require surgery.
3. **Proliferation of lens epithelium** is universal but usually visually inconsequential, since it does not involve the visual axis. It becomes encapsulated within the remnants of the anterior and posterior capsules and is referred to as a Soemmerring ring (Fig. 8.75).
4. **Glaucoma** eventually develops in about 20% of eyes.
   - Closed-angle glaucoma may occur in the immediate postoperative period in microphthalmic eyes secondary to pupil block.
   - Secondary open-angle glaucoma may also develop years after the initial surgery. It is therefore important to monitor the intraocular pressure regularly for many years.
5. **Retinal detachment** is an uncommon and usually late complication.

Visual rehabilitation

Although the technical difficulties of performing cataract surgery in infants and young children have mostly been resolved, visual results continue to be disappointing because of severe and irreversible amblyopia. With regard to optical correction for the aphakic child, the two main considerations are age and laterality of aphakia.

1. **Spectacles** are useful for older children with bilateral aphakia, but not for unilateral aphakia because of associated anisometropia and aniseikonia. Even in infants with bilateral aphakia they may be inappropriate because of their weight, unpleasant appearance, prismatic distortion and constriction of the visual field.
2. **Contact lenses** provide a superior optical solution for both unilateral and bilateral aphakia. Tolerance is usually reasonable until the age of about 2 years, although after this period problems with compliance may start as the child becomes more active and independent. The contact lens may become dislodged or lost, leading to periods of visual deprivation with the risk of amblyopia. In bilateral aphakia, the solution is simply to prescribe spectacles although in unilateral aphakia IOL implantation may have to be considered.
3. **IOL implantation** is increasingly being performed in young children and even infants and appears to be effective and safe in selected cases. Awareness of the rate of myopic shift which occurs in the developing eye, combined with accurate biometry, allows the calculation of an IOL power targeted at initial hypermetropia (correctable with spectacles) which will ideally decay towards emmetropia later in life. However, final refraction is variable and emmetropia in adulthood cannot be guaranteed.
4. **Occlusion** to treat or prevent amblyopia is vital.

Anomalies of lens shape

1. **A lens coloboma** (Fig. 8.76) is characterized by notching (segmental agenesis) at the inferior equator. There is also a corresponding absence of zonular fibres. It is not a true coloboma as there is no focal absence of all tissue layer due to failure of closure of the optic fissure.
2. **Posterior lenticonus** (Fig. 8.77) is a very rare condition characterized by a round or conical bulge of the posterior axial zone of the lens into the vitreous, associated with local thinning or absence of the capsule. It may be associated with opacification of the posterior capsule and hyaloid remnants. With age, the bulge progressively increases in size and the lens cortex may opacify. Progression of cataract is variable, but many cases present with an acutely opacified white lens in infancy or early childhood. Most cases are unilateral, sporadic and not associated with systemic abnormalities. Rarely it may be bilateral and familial.
3. **Anterior lenticonus** (Fig. 8.78) is a bilateral axial projection of the anterior surface of the lens into the anterior chamber. About 90% of patients have Alport syndrome, which may also be associated with cataract, retinal flecks and posterior polymorphous corneal dystrophy.
4. **Lentiglobus** is a very rare, usually unilateral, generalized hemispherical deformity of the lens which may be associated with posterior polar lens opacity.
5. **Microphakia** (Fig. 8.79) is a lens with a smaller than normal diameter. It may be associated with Lowe syndrome, in which the lens is not only small but also disc-like.
6. **Microspherophakia** is a lens with a small diameter and spherical shape.
   a. Causes include familial (dominant) microspherophakia which is not associated with systemic defects, Marfan

Fig. 8.76
Coloboma of the lens

Fig. 8.79
Microphakia

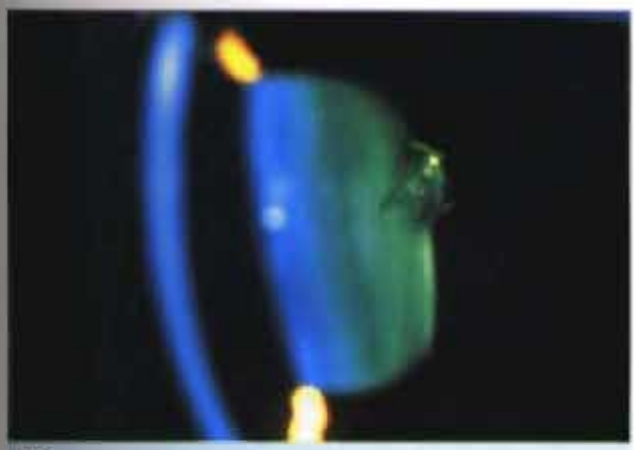

Fig. 8.77
Posterior lenticonus

Fig. 8.80
Microspherophakic lens dislocated into the anterior chamber

Fig. 8.78
Anterior lenticonus (Courtesy of J. Govan)

syndrome, Weill–Marchesani syndrome, hyperlysinaemia and congenital rubella.

b. Ocular associations include Peters anomaly and familial ectopia lentis et pupillae.

c. Complications include lenticular myopia, subluxation and total dislocation into the anterior chamber (Fig. 8.80).

Ectopia lentis

Ectopia lentis refers to a displacement of the lens from its normal position. The lens may be completely dislocated, rendering the pupil aphakic (luxated), or partially displaced, still remaining in the pupillary area (subluxated). Ectopia lentis may be hereditary or acquired. Acquired causes include trauma, a large eye (i.e. high myopia, buphthalmos), anterior uveal tumours and hypermature cataract. Only hereditary causes are discussed below.

Without systemic associations

1. **Familial ectopia lentis** is characterized by bilateral symmetrical superotemporal lenticular displacement,

Inherited in an AD fashion, it may manifest congenitally or later in life.

2. **Ectopia lentis et pupillae** (Fig. 8.81) is a rare, congenital, bilateral, AR disorder characterized by displacement of the pupil and the lens in opposite directions. The pupils are small, slit-like and dilate poorly. Other findings include iris transillumination, enlarged corneal diameter, glaucoma, cataract and microspherophakia.
3. **Aniridia** may occasionally be associated with ectopia lentis.

With systemic associations

1. **Marfan syndrome** is a widespread, autosomal dominant, disorder of connective tissue (*see* Chapter 20) characterized by the following ocular features:
   a. Ectopia lentis, bilateral and symmetrical, is present in 80% of cases. Subluxation is most frequently superotemporal (Fig. 8.82), but may be in any meridian. Because the zonule is frequently intact, accommodation is retained, although rarely the lens may dislocate into the anterior chamber or vitreous (Fig. 8.83). The lens also may be microspherophakic.

Fig. 8.81
Ectopia lentis et pupillae

Fig. 8.82
Upward lens subluxation in Marfan syndrome

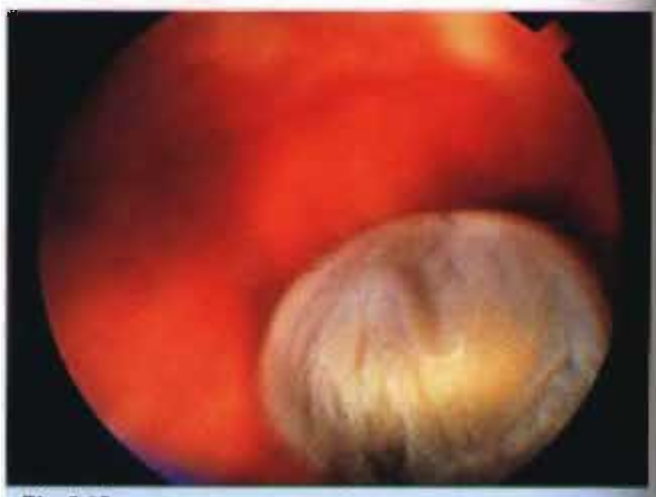

Fig. 8.83
Dislocation of the lens into the vitreous in Marfan syndrome
(Courtesy of S. Milewski)

   b. Angle anomaly is present in 75% of eyes. It is characterized by dense iris processes and thickened trabecular sheets, and may be responsible for glaucoma.
   c. Retinal detachment associated with lattice degeneration and high axial myopia is the most serious complication.
   d. Other features include hypoplasia of dilator pupillae (rendering mydriasis difficult), peripheral iris transillumination, strabismus, flat cornea and blue sclera.
2. **Weili–Marchesani syndrome** is a rare systemic connective tissue disease, conceptually the converse of Marfan syndrome, characterized by short stature, brachydactyly with stiff joints and mental handicap. Inheritance may be AD or AR.
   a. Ectopia lentis, bilateral and inferior, occurs in about 50% of cases during the 'teens' or early twenties. Microspherophakia is frequent.
   b. Secondary angle-closure glaucoma may occur due to pupillary block, consequent upon spherophakia and forward movement of the lens, although there may be a congenital angle anomaly.
   c. Other features include asymmetrical axial lengths and presenile vitreous liquefaction.
3. **Homocystinuria** is an AR inborn error of metabolism in which decreased hepatic activity of cystathionine β-synthetase results in systemic accumulation of homocysteine and methionine. Systemic features include skeletal anomalies with a Marfanoid habitus, fair hair and a tendency to thrombotic episodes.
   a. Ectopia lentis, typically inferonasal (Fig. 8.84), usually occurs by the age of 10 years. The zonule, which normally contains high levels of cysteine, disintegrates so that accommodation is often lost.
   b. Secondary angle-closure glaucoma may occur as a result of pupil block caused by lens incarceration in the pupil, or a total dislocation into the anterior chamber.
4. **Hyperlysinaemia** is a very rare, AR, inborn error of metabolism caused by a deficiency in lysine alpha-

Fig. 8.84
Inferonasal lens subluxation in homocystinuria

ketoglutarate reductase. Systemic features include lax ligaments, hypotonic muscles, seizures and mental handicap. It is occasionally associated with ectopia lentis.

5. **Sulphite oxidase deficiency** is a very rare, AR disorder of sulphur metabolism characterized by progressive muscular rigidity, decerebrate posture, mental handicap and demise usually before the age of 5 years. Ectopia lentis is universal.
6. **Stickler syndrome** is occasionally associated with ectopia lentis, retinal detachment being the most common problem (*see* Chapter 12).
7. **Ehlers–Danlos syndrome** (*see* Chapter 20) is occasionally associated with ectopia lentis.

Management

The main complications of ectopia lentis are (a) refractive error (lenticular myopia), (b) optical distortion due to astigmatism and/or lens edge effect, (c) glaucoma and, rarely, (d) lens-induced uveitis.

1. **Spectacle correction** may correct astigmatism induced by lens tilt or edge effect in eyes with mild subluxation. Aphakic correction may also afford good visual results if a significant portion of the visual axis is aphakic in the undilated state.
2. **Surgical removal** of the lens, using closed intraocular microsurgical techniques, is indicated for cataract, lens-induced glaucoma, uveitis or endothelial touch.

CHAPTER 9

Glaucoma

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Introduction

Physiology of aqueous production

The ciliary body consists of the anterior pars plicata (2 mm wide) and the posterior pars plana (4 mm wide). The pars plicata bears 70 radially orientated ciliary processes which project into the posterior chamber. Each ciliary process is lined by a pigmented epithelial layer continuous with the retinal pigment epithelium and a non-pigmented epithelial layer continuous with the neuroretina. Each process also has a central arteriole ending in a rich capillary network. Tight junctions between adjacent non-pigmented epithelial cells constitute the blood–aqueous barrier. Aqueous humour is actively secreted by the non-pigmented epithelium as a result of a metabolic process that depends on several enzyme systems, especially the Na^+/K^+-ATPase pump, which secretes Na^+ ions into the posterior chamber. Water follows passively along the osmotic gradient. Carbonic anhydrase also plays a role, but the precise mechanism is uncertain. Aqueous secretion is diminished by factors that inhibit active metabolism such as hypoxia and hypothermia but it is independent of the level of intraocular pressure (IOP). Analysis of the hydrostatic and osmotic pressures across the ciliary epithelium reveals that under normal conditions passive secretion plays little, if any, role in the genesis of aqueous humour. Aqueous secretion is diminished by the following:

- Drugs such as beta-blockers, sympathomimetics and carbonic anhydrase inhibitors.
- Cyclodestructive procedures such as cyclocryotherapy and laser ablation.
- Ciliary body shutdown which may be caused by: detachment of the ciliary body, inflammation of the secretory ciliary epithelium associated with iridocyclitis and retinal detachment.

Fig. 9.1
Scanning electron micrograph of the trabecular meshwork

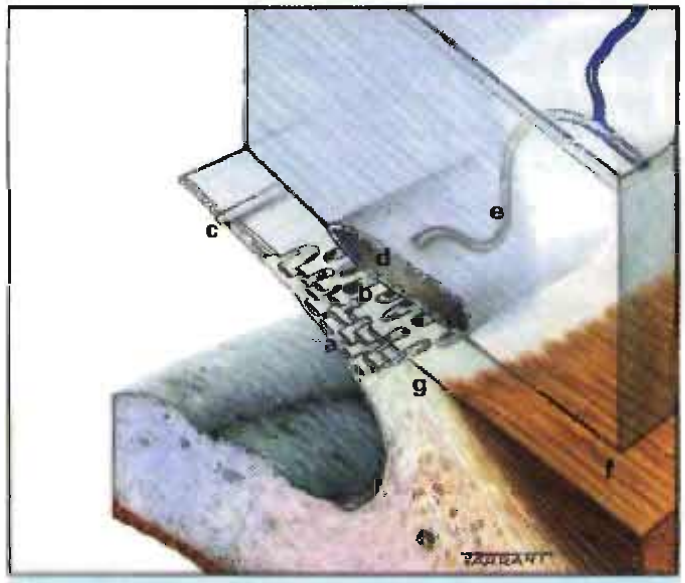

Fig. 9.2
Anatomy of the outflow channels. (a) Uveal meshwork; (b) corneoscleral meshwork; (c) Schwalbe line; (d) Schlemm canal; (e) collector channels; (f) longitudinal muscle of the ciliary body; (g) scleral spur

Aqueous outflow

Anatomy

1. The **trabecular meshwork** (trabeculum) is a sieve-like structure at the angle of the anterior chamber, through which 90% of the aqueous humour leaves the eye (Fig. 9.1). It consists of the following three portions:
   a. ***The uveal meshwork*** (Fig. 9.2a) is the innermost portion, which consists of cord-like meshes that extend from the root of the iris to Schwalbe line (Fig. 9.2c). The intertrabecular spaces are relatively large and offer little resistance to the passage of aqueous.
   b. ***The corneoscleral meshwork*** (Fig. 9.2b) forms the larger middle portion which extends from the scleral spur (Fig. 9.2g) to Schwalbe line. The meshes are sheet-like and the intertrabecular spaces are smaller than in the uveal meshwork.
   c. ***The endothelial (juxtacanalicular) meshwork*** is the outer part of the trabeculum which links the corneoscleral meshwork with the endothelium of the inner wall of Schlemm canal (Fig. 9.2d). The juxtacanalicular tissue offers the major proportion of normal resistance to aqueous outflow.
2. **Schlemm canal** is a circumferential channel in the perilimbal sclera, bridged by septa. The inner wall of the canal is lined by irregular spindle-shaped endothelial cells which contain infoldings (giant vacuoles). The outer wall of the canal is lined by smooth flat cells and contains the openings of the collector channels (Fig. 9.2e) which leave Schlemm canal at oblique angles and connect directly or indirectly with episcleral veins.

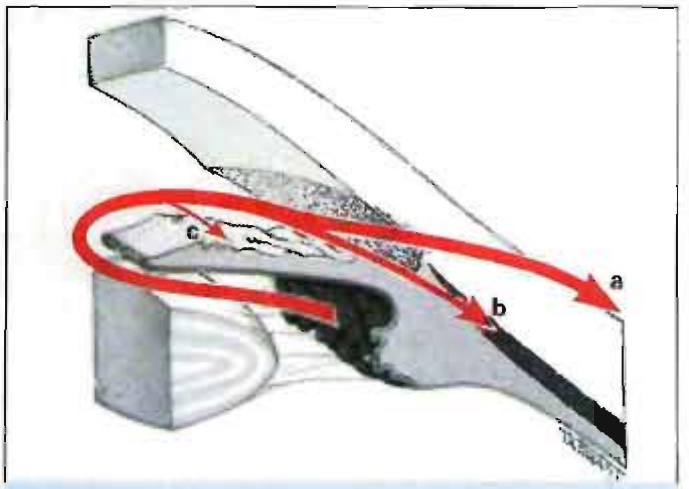

Fig. 9.3
Normal outflow of aqueous humour. (a) Conventional trabecular route; (b) uveoscleral route; (c) through the iris

Physiology

Aqueous flows from the posterior chamber via the pupil into the anterior chamber, from where it exits the eye by two different routes:

1. **Trabecular (conventional) route** accounts for approximately 90% of aqueous outflow (Fig. 9.3a). The aqueous flows through the trabeculum into Schlemm canal and is then drained by the episcleral veins. This is a bulk-flow pressure-sensitive route so that increasing the pressure head will increase outflow. Trabecular outflow can be increased by drugs (miotics, sympathomimetics), laser trabeculoplasty and trabeculotomy.
2. **Uveoscleral (unconventional) route** accounts for the remaining 10% of aqueous outflow (Fig. 9.3b). The aqueous passes across the face of the ciliary body into the suprachoroidal space and is drained by the venous circulation in the ciliary body, choroid and sclera. Uveoscleral outflow is decreased by miotics and increased by atropine, sympathomimetics and prostaglandins. Some aqueous also drains via the iris (Fig. 9.3c)

Intraocular pressure

Determining factors

1. **Rate of aqueous secretion.**
2. **Rate of aqueous outflow**, which is in turn related to the resistance encountered in the outflow channels and the level of episcleral venous pressure. The rate of aqueous outflow is proportional to the difference between the intraocular and episcleral venous pressure. The relationship between these factors can be expressed as follows:

$F = C\,(Po - Pe)$ where:

F = rate of aqueous outflow (normal 2 µl/min)
C = facility of aqueous outflow (normal 0.2 µl/min per mmHg)
Po = IOP in mmHg
Pe = episcleral venous pressure (normal 10 mmHg)

For example:

- If episcleral venous pressure is 20 mmHg the IOP will be $(2/0.2) + 20 = 30$ mmHg.
- If the facility of outflow is 0.05 the IOP will be $(2/0.05) + 10 = 50$ mmHg.

Distribution

The distribution of IOP within the general population has a range of 11–21 mmHg. Although there is no absolute cut-off point, 21 mmHg is considered the upper limit of normal and levels above this are viewed with suspicion. However, in some patients glaucomatous damage occurs with IOPs less than 21 mmHg (normal-tension glaucoma), while others remain unscathed with IOPs up to 30 mmHg (ocular hypertension). Although the actual level of IOP is important in the development of glaucomatous damage, other factors also play a part. The level of IOP is inherited so that first-degree relatives of patients with primary open-angle glaucoma have higher IOPs.

Fluctuation

Normal IOP varies with the time of day, heartbeat, blood pressure level and respiration. The pattern of diurnal curve of IOP varies, with a tendency to be higher in the morning and lower in the afternoon and evening. Normal eyes manifest a mean diurnal pressure variation of 5 mmHg; ocular hypertensive or glaucomatous eyes, however, exhibit a wider fluctuation. In normal-tension glaucoma the fluctuations are the same as in normals. A single normal reading, particularly if taken during late afternoon, may therefore be misleading and it may be necessary to take several readings at different times of day (phasing). In clinical practice phasing during the morning hours may be sufficient because 80% of patients peak between 8 and 12 a.m.

Classification

Glaucoma is an optic neuropathy with characteristic appearances of the optic disc and specific pattern of visual field defects that is associated frequently but not invariably with raised IOP. Because the pathophysiology, clinical presentation and treatment of the different types of glaucoma are so varied, there is no single definition that adequately encompasses all forms. Understanding this concept helps to explain, for example, why one patient with 'glaucoma' may have no symptoms while another experiences sudden pain and redness. Glaucoma may be (a) *congenital* (developmental) or (b) *acquired*. Further subclassification into open-angle and angle-closure types is based on the mechanism by which aqueous outflow is impaired. The glaucoma may also be (a) *primary* or (b) *secondary* depending on the presence or absence of associated factors contributing to the pressure rise. In primary glaucomas the elevation of IOP is not

associated with any other ocular disorder whereas in secondary glaucomas a recognizable ocular or non-ocular disorder alters aqueous outflow which, in turn, results in elevation of IOP. Secondary glaucomas may be acquired or developmental and of the open-angle or angle-closure type.

Secondary open-angle glaucomas

They can be subdivided on the basis of the site of aqueous outflow obstruction.

1. **Pre-trabecular** glaucoma in which aqueous outflow is obstructed by a membrane covering the trabeculum (Fig. 9.4a), which may consist of:
   - Fibrovascular tissue (e.g. neovascular glaucoma).
   - Endothelial cells (e.g. iridocorneal endothelial syndrome).
   - Epithelial cells (e.g. epithelial ingrowth).
2. **Trabecular** glaucoma in which the obstruction occurs as a result of 'clogging up' of the meshwork by:
   - Pigment particles (e.g. pigmentary glaucoma, Fig. 9.4b).
   - Red blood cells (e.g. red cell glaucoma).
   - Degenerated red cells (e.g. ghost cell glaucoma).
   - Macrophages and lens proteins (e.g. phacolytic glaucoma).
   - Proteins (e.g. hypertensive uveitis).
   - Pseudoexfoliative material (e.g. pseudoexfoliation glaucoma).

   Trabecular glaucomas may also be caused by alteration of the trabecular fibres themselves by:
   - Oedema (e.g. herpes zoster iritis).
   - Scarring (e.g. post-traumatic angle recession glaucoma).
3. **Post-trabecular** glaucoma in which the trabeculum itself is normal but aqueous outflow is impaired as a result of elevated episcleral venous pressure due to:
   - Carotid–cavernous fistulae.
   - Sturge–Weber syndrome.
   - Obstruction of the superior vena cava.

Secondary angle-closure glaucomas

These are caused by impairment of aqueous outflow secondary to apposition between the peripheral iris and the trabeculum by either posterior or anterior forces as follows:

1. **Posterior forces** push the peripheral iris against the trabeculum (e.g. iris bombé due to seclusio pupillae, (Fig. 9.4c)).
2. **Anterior forces** pull the iris over the trabeculum by contraction of inflammatory (Fig. 9.4d) or fibrovascular membranes (e.g. late neovascular glaucoma).

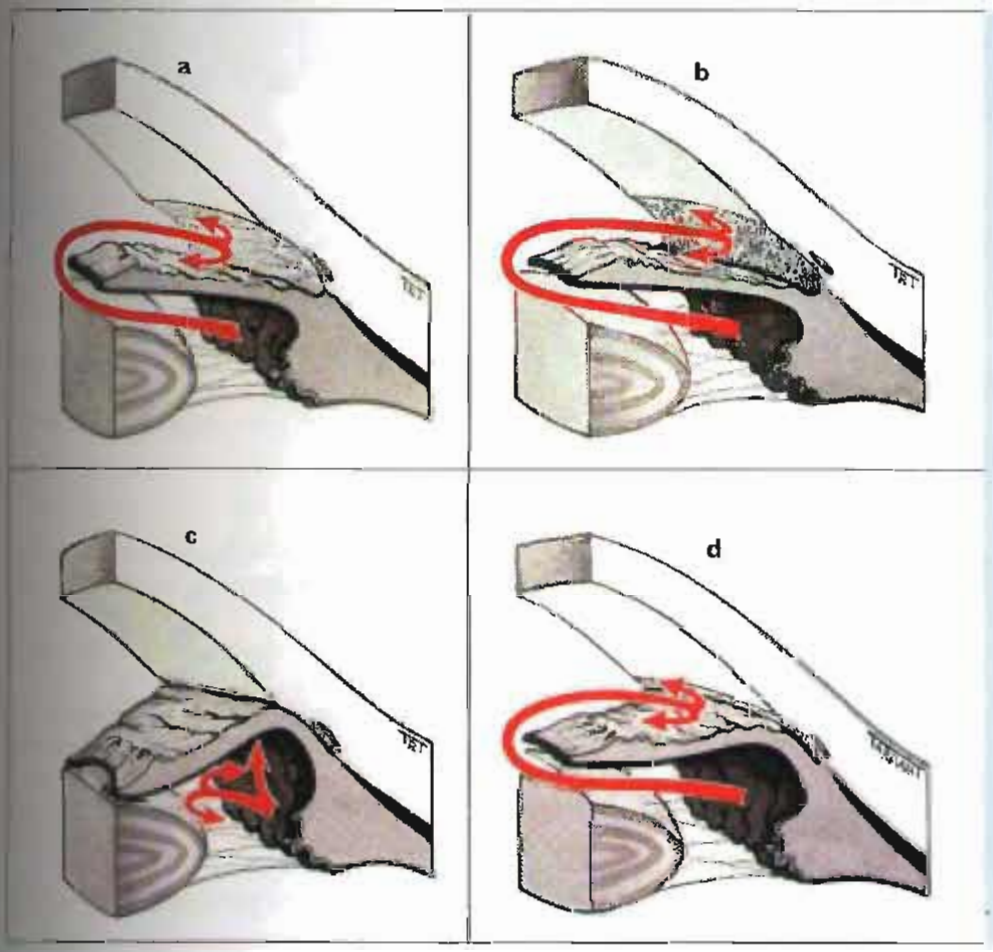

Fig. 9.4
Mechanism of aqueous obstruction in secondary glaucomas (see text)

Tonometry

Goldmann tonometry

General principles

Tonometry is the objective measurement of IOP, based, most commonly, on the force required to flatten the cornea, or the degree of corneal indentation produced by a fixed force. Applanation tonometry is based on the Imbert–Fick principle, which states that for an ideal, dry, thin-walled sphere, the pressure inside the sphere (P) equals the force necessary to flatten its surface (F) divided by the area of flattening (A) (i.e. $P = F/A$). The IOP is proportional to the pressure applied to the globe (in practice the cornea) and the thickness of the walls of the globe (i.e. the thickness of the cornea, which is variable). The human eye is, however, not an ideal sphere—the cornea is rigid and resists flattening. Capillary attraction of the tear meniscus however, tends to pull the tonometer towards the cornea. Corneal rigidity and capillary attraction cancel each other when the flattened area has a diameter of 3.06 mm, as in Goldmann tonometry (Fig. 9.5). The Goldmann tonometer is a very accurate variable-force tonometer consisting of a double prism (Fig. 9.6).

Procedure

1. Topical anaesthetic and fluorescein are instilled into the conjunctival sac.
2. At the slit-lamp, a Goldmann prism (mounted on a tonometer) is applied axially to the cornea surface.
3. A pattern of two semicircles will be seen, one above and one below the horizontal midline.

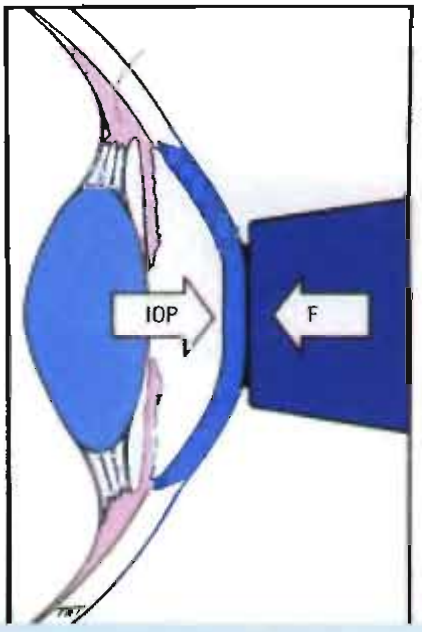

Fig. 9.5
Principles of Goldmann applanation tonometry

Fig. 9.6
Goldmann applanation tonometer

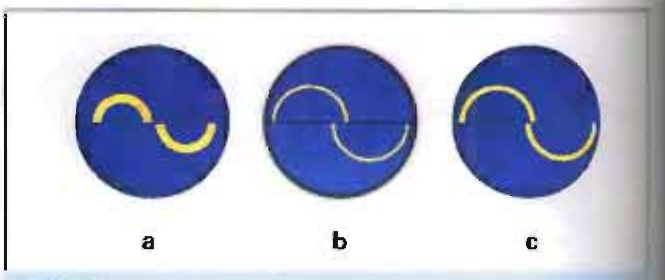

Fig. 9.7
Fluorescein-stained semicircles seen during tonometry (see text)

4. The dial on the tonometer is rotated to align the inner margins of the semicircles (Fig. 9.7c).
5. The reading on the dial, multiplied by 10, equals the IOP.

Potential errors

1. **Inappropriate fluorescein pattern** resulting from excessive fluorescein will make the semicircles too thick and the radius too small (Fig. 9.7a), whereas insufficient fluorescein will make the semicircles too thin and the radius too large (Fig. 9.7b).
2. **Pressure on the globe**, from the examiner's fingers or by the patient squeezing the eyelids (Fig. 9.8) will result in an artificially high reading.
3. **Incorrect calibration** of the tonometer can result in an incorrect reading. It is therefore important to check the calibration at regular intervals.
4. **Corneal pathology** such as gross oedema, distortion and abnormal thickness will result in inaccurate readings.

Fig. 9.8
Squeezing of the eyelids during tonometry will result in an inaccurate reading

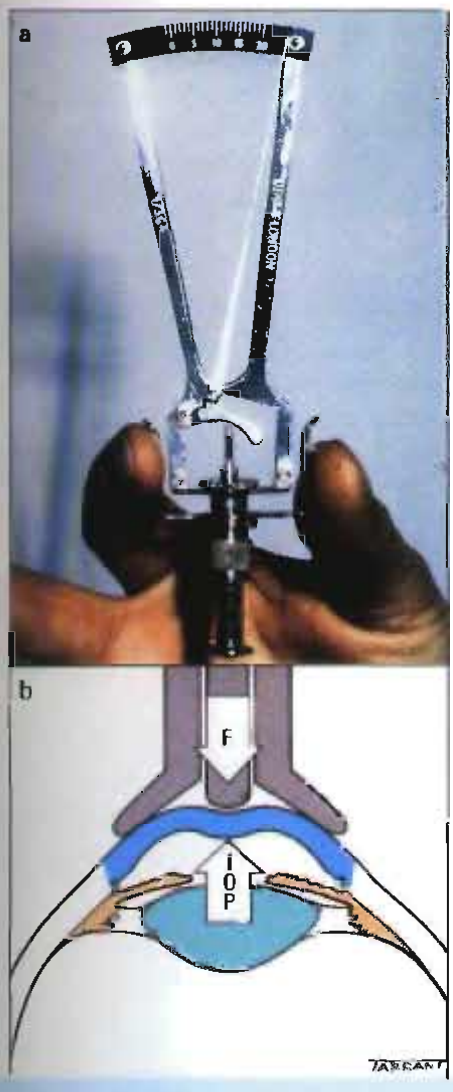

Fig. 9.9
(a) Schiotz tonometer; (b) principles of indentation tonometry

Other tonometers

1. **The Schiotz** relies on the principle of indentation tonometry in which a plunger with a pre-set weight indents the cornea (Fig. 9.9). The amount of indentation is measured on a scale and the reading is converted into millimetres of mercury on a special table. The tonometer is cheap, easy to use and does not require a slit-lamp but is now seldom used.
2. **The Perkins** is a hand-held applanation tonometer which uses a Goldmann prism adapted to a small light source. It is small, does not require a slit-lamp and can therefore be used in bed-bound or anaesthetized patients (Fig. 9.10). It does, however, require considerable practice before reliable readings can be obtained.
3. **The air-puff** (Fig. 9.11) is a non-contact tonometer based on the principle of applanation but, instead of using a prism, the central part of the cornea is flattened by a jet of air. The time required to sufficiently flatten the cornea relates directly to the level of IOP. The instrument is easy to use and does not require topical anaesthesia. It is therefore

Fig. 9.10
Perkins hand-held applanation tonometer

Fig. 9.11
Air-puff tonometer

Fig. 9.12
Pulsair (Keeler) tonometer

Fig. 9.13
Tono-Pen

particularly useful for screening by non-ophthalmologists. Its main disadvantage is that it is accurate only within the low-to-middle range. The jet of air can startle the patient both with its apparent force and noise.

4. **The Pulsair 2000 Keeler** (Fig. 9.12) is a hand-held non-contact tonometer, incorporating an automatic alignment activation device which reduces user error. The instrument can be used with the patient in the upright and supine positions and does not make a noise. It provides clinically useful measurements comparable with Goldmann tonometry although with use a tendency to a long-term drift in accuracy mandates regular re-calibration.
5. **The Tono-Pen** is a hand-held, self-contained, battery powered, portable, contact tonometer (Fig. 9.13). The probe tip contains a transducer that measures the applied force. A microprocessor analyses the force/time curve generated by the transducer during corneal indentation to calculate IOP. The instrument correlates well with Goldmann tonometry although it slightly overestimates a low IOP and underestimates a high IOP. Its main advantage involves the ability to measure IOP in eyes with distorted or oedematous corneas, as well as through a bandage contact lens.

Gonioscopy

Introduction

Purposes

The angle between the posterior corneal surface and the anterior surface of the iris constitutes the angle of the anterior chamber, the configuration of which is relevant to the pathogenesis of glaucoma. Contact between peripheral iris and cornea signifies a closed angle, which precludes aqueous access to the trabecular meshwork, while wide separation between the two signifies an open angle, implying that the obstruction to aqueous outflow lies in or beyond the trabecular meshwork. Gonioscopy involves the examination and analysis of the angle.

1. **Diagnostic** gonioscopy facilitates the identification of abnormal angle structures and estimation of the width of the chamber angle, particularly important in the management of eyes with narrow angles.
2. **Surgical** gonioscopy involves visualization of the angle during procedures such as laser trabeculoplasty and goniotomy.

Optical principles

The angle of the anterior chamber cannot be visualized directly through the intact cornea because light emitted from angle structures undergoes total internal reflection at the anterior surface of the precorneal tear film. A goniolens eliminates total internal reflection by replacing the tear film–air interface with a new tear film–goniolens interface (Fig. 9.14).

1. **Indirect** goniolenses (goniomirrors) provide a mirror image of the opposite angle and can be used only in conjunction with a slit-lamp.

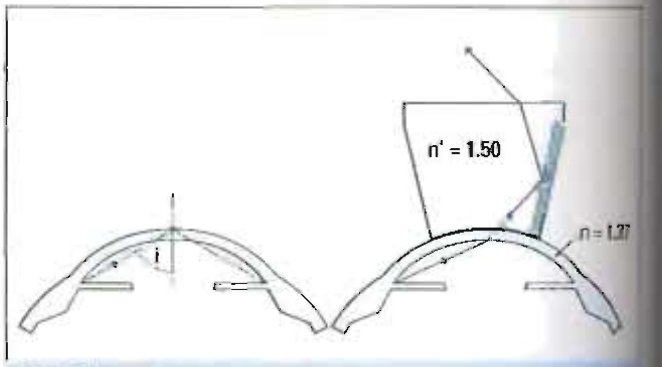

Fig. 9.14
Optical principles of gonioscopy: n = refractive index; i = angle of incidence

2. **Direct** goniolenses (gonioprisms) provide a direct view of the angle. They do not require a slit-lamp and are used with the patient in the supine position.

Goniolenses

Goldmann three-mirror

This is an indirect goniolens with a contact surface diameter of approximately 12 mm (Fig. 9.15 left). Relatively easy to use, it affords an excellent view of the angle. It also stabilizes the globe and is therefore suitable for argon laser trabeculoplasty. Because the curvature of the contact surface of the lens is steeper than that of the cornea a viscous coupling substance with the same refractive index as the cornea is required to bridge the gap between the cornea and the goniolens. Following the use of the coupling substance the patient's vision is blurred and fundus examination impaired. Perimetry, ophthalmoscopy or photography of the disc should therefore be performed before gonioscopy.

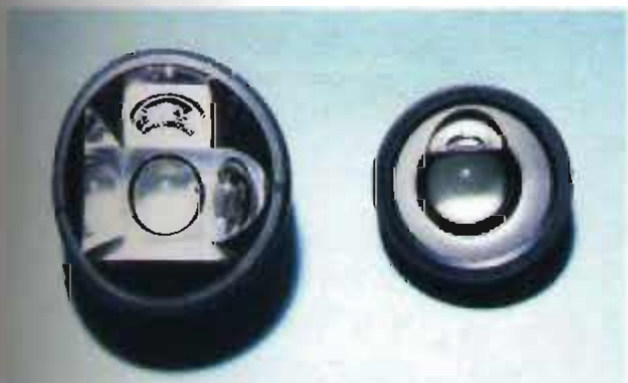

Fig. 9.15
(a) Goldmann triple-mirror lens; (b) single-mirror goniolens

Fig. 9.16
Zeiss four-mirror goniolens

Modifications of the Goldmann lens with one (Fig. 9.15 right) and two mirrors and antireflective coating have been designed for laser trabeculoplasty, enabling simultaneous visualization of a wider circumference of the angle.

Zeiss

This and the similar Posner and Sussman, are indirect four-mirror goniolenses mounted on a handle (Fig. 9.16). The contact surface of the lens has a diameter of 9 mm and a curvature flatter than that of the cornea, negating the need for a coupling substance. Tears provide adequate contact material and lubrication for the lens. This permits quick and comfortable examination of the angle and, importantly, does not interfere with subsequent examinations of the fundus. The four mirrors enable the entire circumference of the angle to be visualized with minimal rotation. This lens is useful for indentation gonioscopy (*see* below), but because it does not stabilize the globe it cannot be used for laser trabeculoplasty.

Koeppe

This is a dome-shaped direct diagnostic goniolens which comes in several sizes (Fig. 9.17). It is easy to use and provides a panoramic view of the angle. It is therefore particularly

Fig. 9.17
Koeppe goniolenses

Fig. 9.18
Swan–Jacob surgical goniolens

useful for simultaneous comparison of one portion of the angle with another. Moreover, with the patient in the supine position the anterior chamber may become slightly deeper and the angle easier to visualize. When used in conjunction with a hand-held microscope, it offers great flexibility, allowing detailed inspection of the various subtleties of angle structures both by direct and retroillumination. It cannot be used in conjunction with a slit-lamp and therefore does not provide the same clarity, illumination and variable powers comparable with slit-lamp goniolenses.

Swan–Jacob

This is a direct surgical goniolens which is held on the cornea by a handle (Fig. 9.18).

Gonioscopic technique

Goldmann gonioscopy

The patient should be advised that the lens will touch the eye but not cause more than slight discomfort. The patient should also be requested to keep both eyes open at all times and not to move the head backwards when the lens is being inserted.

1. Topical anaesthetic is instilled into the lower fornix.
2. A coupling fluid (e.g. a carbomer gel) is inserted into the cup of the lens but it should be no more than half full.
3. The patient looks up and the inferior rim of the lens is inserted into the lower fornix and then pressed quickly against the cornea so that the coupling substance does not escape. The patient is then asked to gaze straight ahead with the other eye.
4. The angle is visualized with the small dome-shaped gonioscopic mirror (if a three-mirror lens is being used).
5. Initially the mirror is placed at the 12 o'clock position to visualize the inferior angle and then rotated clockwise. The slit beam should be 2 mm wide and when viewing different positions it is usually best to rotate the beam so that its axis is at right angles to the mirror.

> ***NB:*** The image is laterally reversed with the mirror in the horizontal meridian and vertically inverted when in the vertical meridian.

Zeiss gonioscopy

The preliminary steps are the same as for Goldmann gonioscopy but a coupling fluid is not required.

1. The patient looks straight ahead. Under slit-lamp visualization the lens is placed directly on the centre of the cornea. Only gentle contact with the cornea is needed because excessive pressure will inadvertently distort angle structures.
2. Each quadrant of the angle is visualized with the opposite mirror. The central fundus may be viewed through the centre of the lens.
3. Indentation gonioscopy may be performed by pressing posteriorly against the cornea. This will force aqueous into the angle of the anterior chamber, forcing the peripheral iris posteriorly.
   - If the angle is closed by mere apposition between the iris and cornea (appositional closure), the angle will be forced open, allowing visualization of the angle recess (Fig. 9.19b).
   - If the angle is completely closed by adhesions between the peripheral iris and cornea (synechial closure) it will remain closed (Fig. 9.19c).

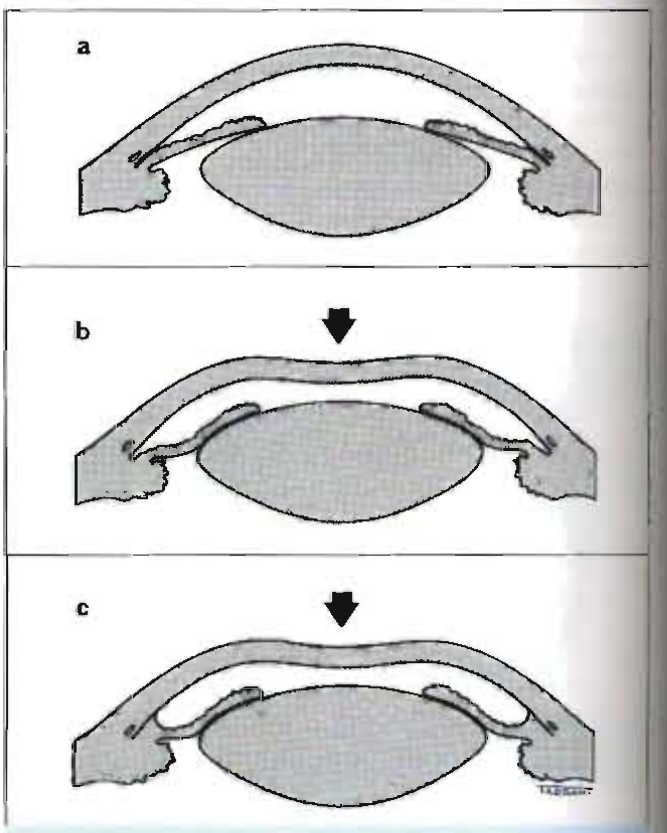

Fig. 9.19
Principles of indentation gonioscopy (see *text*)

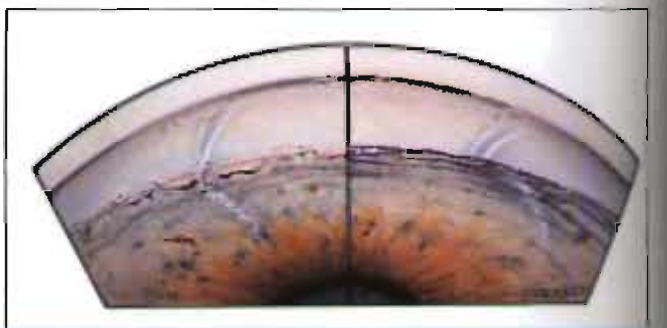

Fig. 9.20
Indentation gonioscopy. **(Right)** appearance of the angle before indentation showing complete closure and inability to visualize the apex of the corneal wedge; **(left)** during indentation part of the angle is forced open but some permanent peripheral synechiae remain

- If synechial closure is partial, part of the angle will open and a part will remain closed (Fig. 9.20 left).

NB: With practice, gentle indentation gonioscopy allows better visualization even of the normal angle. Goniolenses are a potential source of infection and should be disinfected in the same way as tonometer heads.

Identification of angle structures

Figure 9.21 shows the anatomy of angle structures.

1. **Schwalbe line** is the most anterior structure, appearing as an opaque line. Anatomically it demarcates the peripheral termination of Descemet membrane and the anterior limit of the trabeculum.
2. **The corneal wedge** is useful in locating an inconspicuous Schwalbe line as follows:
   a. Using a narrow slit beam, two linear reflections can be seen, one from the external surface of the cornea and its junction with the sclera, the other from the internal surface of the cornea.
   b. The two reflections meet at the apex of the corneal wedge, which coincides with Schwalbe line.

NB: When performing laser trabeculoplasty a pigmented Schwalbe line should not be confused with the posterior pigmented trabeculum.

3. **The trabeculum** extends from Schwalbe line to the scleral spur and has an average width of 600 μm. Gonioscopically, it has a ground-glass appearance and appears to have depth. The anterior non-functional part lies adjacent to Schwalbe line and has a whitish colour. The posterior functional pigmented part lies adjacent to the scleral spur and has a greyish-blue translucent appearance. In laser trabeculoplasty burns are applied at the junction of the non-pigmented and pigmented trabeculum. Trabecular pigmentation (Fig. 9.22) is rare prior to puberty. In ageing eyes it involves the posterior trabeculum to a variable extent, most marked inferiorly and least in the horizontal meridian. Trabecular pigmentation is also most marked in brown eyes. Pathological hyperpigmentation is caused by excessive shedding of pigment from the posterior layer of the iris in the following conditions:
   - Pigment dispersion syndrome.
   - Pseudoexfoliation syndrome.
   - Blunt ocular trauma.
   - Anterior uveitis.
   - Following acute angle-closure glaucoma.
   - Diabetes (especially after cataract surgery).
   - Naevus of Ota.
4. **Schlemm canal** may be identified in the non-pigmented angle as a slightly darker line deep to the posterior trabeculum. Blood can sometimes be seen in this canal if the goniolens compresses the episcleral veins such that the episcleral venous pressure exceeds the IOP. Pathological causes of raised episcleral venous pressure which may be associated with blood in Schlemm canal include:
   - Carotid–cavernous fistula and dural shunt.
   - Sturge–Weber syndrome.
   - Obstruction of the superior vena cava.
5. **The scleral spur** is the anterior-most projection of the sclera and the site of attachment of the longitudinal muscle of the ciliary body. Gonioscopically, the scleral spur is situated immediately posterior to the trabeculum and appears as a narrow, dense, often shiny, whitish band. It is the most important landmark because it has a relatively consistent appearance in different eyes.

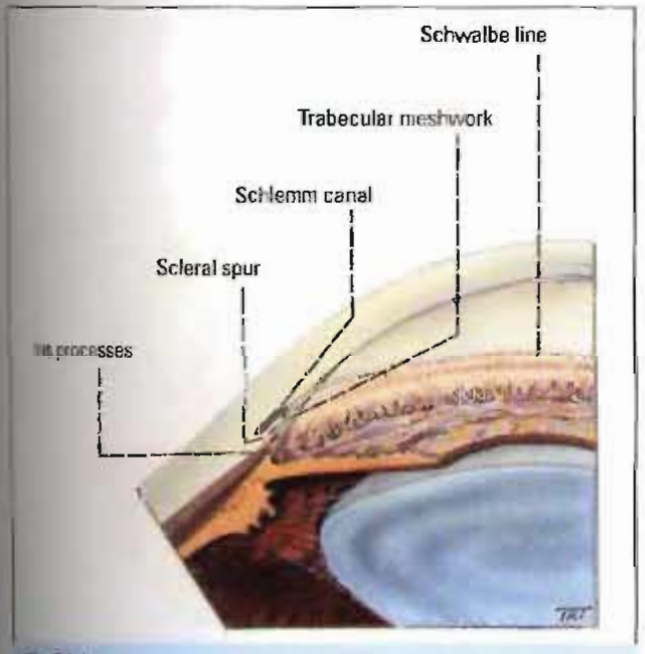

Fig. 9.21
Anatomy of the angle structures

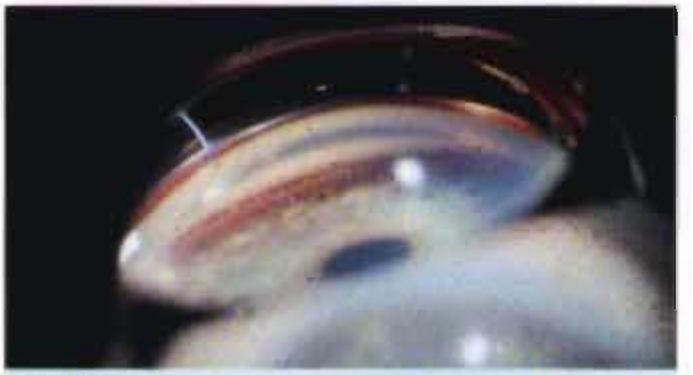

Fig. 9.22
Wide open angle with trabecular pigmentation

NB: In laser trabeculoplasty it is important to identify the scleral spur because the application of burns posterior to it will result in greater inflammation, with consequent increased risk of early post-laser rise in IOP and the formation of peripheral anterior synechiae.

6. **The ciliary body** stands out just behind the scleral spur as a pink to dull-brown to slate-grey band. Its width depends on the position of iris insertion and it tends to be narrower in hypermetropic eyes and wider in myopic eyes. The angle recess represents the posterior dipping of the iris as it inserts into the ciliary body.
7. **Iris processes** are small extensions of the anterior surface of the iris which insert at the level of the scleral spur and cover the ciliary body in varying degrees. They are present in about one-third of normal eyes and are most prominent during childhood and in brown eyes. With increasing age they tend to wither and lose their continuity. Iris processes should not be confused with peripheral anterior synechiae, which are broader and represent adhesions between the iris and angle structures. However, fine stellate peripheral anterior synechiae induced by inappropriate laser trabeculoplasty may easily be mistaken for iris processes.
8. **Blood vessels** running in a radial pattern at the base of the angle recess are often seen in normal eyes. Pathological blood vessels, which run randomly in various directions, occur in:
   - Neovascular glaucoma.
   - Fuchs uveitis syndrome.
   - Chronic anterior uveitis.

Grading of angle width

Grading of angle width is essential to the assessment of the glaucomatous or potentially glaucomatous eye. The main aims are to evaluate the functional status of the angle, the degree of closure and the risk of future closure. The following features should be noted and described in the superior and inferior halves of the angle, bearing in mind that most angles are narrowest superiorly.

- The shape and contour of the peripheral iris.
- The deepest structure seen.
- Amount of trabecular pigmentation.
- Presence of peripheral anterior synechiae.

The Shaffer system (Fig. 9.23) records the angle in degrees of arc subtended by two imaginary tangential lines drawn to the inner surface of the trabeculum and the anterior surface of the iris about one-third of the distance from its periphery. In practice, the angle is graded according to the visibility of various angle structures. The system assigns a numerical grade (4–0) to each angle with associated anatomical description, angle width in degrees and implied clinical interpretation.

1. **Grade 4** (35–45°) is the widest angle characteristic of myopia and aphakia in which the ciliary body can be visualized with ease: it is incapable of closure.
2. **Grade 3** (25–35°) is an open angle in which at least the scleral spur can be identified: it is also incapable of closure.
3. **Grade 2** (20°) is a moderately narrow angle in which only the trabeculum can be identified; angle closure is possible but unlikely.
4. **Grade 1** (10°) is a very narrow angle in which only Schwalbe line, and perhaps also the top of the trabeculum, can be identified: angle closure is not inevitable but the risk is high.
5. **Slit angle** is one in which there is no obvious iridocorneal contact but no angle structures can be identified; this angle has the greatest danger of imminent closure.
6. **Grade 0** (0°) is a closed angle due to iridocorneal contact and is recognized by the inability to identify the apex of the corneal wedge. Indentation gonioscopy with a Zeiss goniolens is necessary to differentiate 'appositional' from 'synechial' angle closure as previously described.

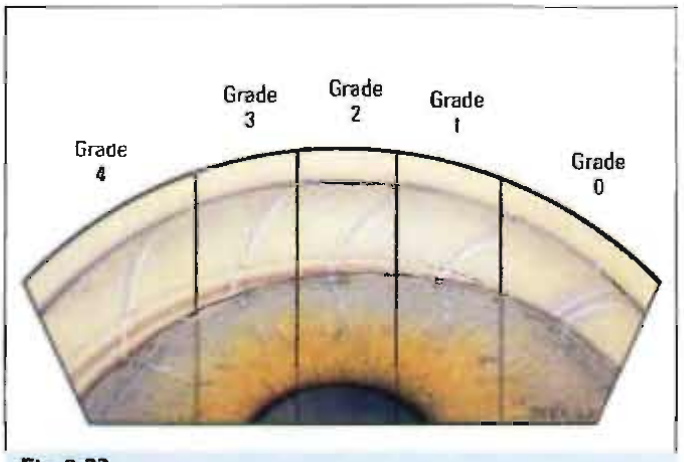

Fig. 9.23
Shaffer grading of angle width

The optic nerve head

Applied anatomy

Retinal nerve fibres

An understanding of the distribution of the 1.2 million ganglion cell axons as they pass across the retina to enter the

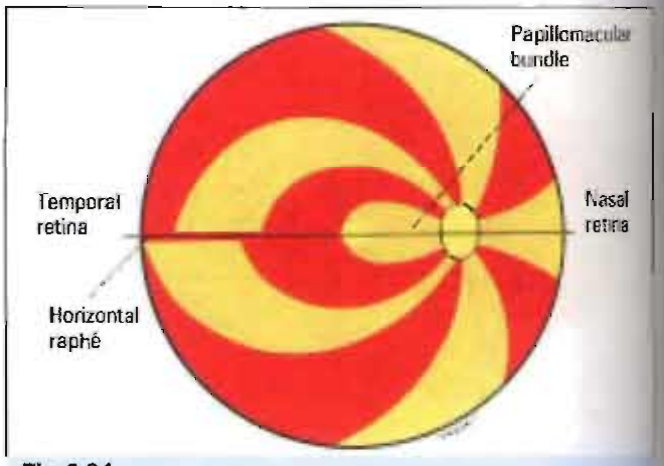

Fig. 9.24
Anatomy of retinal nerve fibres

scleral canal to form the optic nerve head (optic disc) is the key to the interpretation of visual field loss in relation to optic nerve cupping in glaucoma.

1. **Within the retina** the arrangement is as follows (Fig. 9.24):
   - Fibres arising from the macula follow a straight course to the optic nerve head, forming a spindle-shaped area (papillomacular bundle).
   - Fibres arising from the nasal retina also follow a relatively straight course to the optic nerve.
   - Fibres arising temporal to the macula follow an arcuate path around the papillomacular bundle to reach the optic nerve head. They do not cross the horizontal raphé that extends from the foveola to the temporal retinal periphery, demarcating the superior and inferior halves of the retina.

> **NB:** The arcuate fibres reaching the superotemporal and inferotemporal aspects of the optic nerve head are most vulnerable to glaucomatous damage; the fibres in the papillomacular bundle are the most resistant.

2. **Within the optic nerve head** the retinal fibres are arranged as follows (Fig. 9.25):
   - Fibres from the peripheral fundus lie deep within the retinal nerve fibre layer (i.e. nearer the pigment epithelium) but occupy the most peripheral (superficial) portion of the optic nerve.
   - Fibres arising near to the optic nerve lie superficially within the nerve fibre layer (i.e. nearer the vitreous) but they occupy the central (deep) portion of the optic nerve.

Optic nerve head

1. **The posterior scleral foramen** (scleral canal) is the conduit for the retinal nerve fibres leaving the eye. It is usually oval in its vertical axis and has an average vertical diameter of 1.75 mm, which is, however, related to the size of the optic disc and the globe itself. Eyes with small canals therefore have small optic discs (e.g. hypermetropia) and those with large canals have large discs (e.g. myopia). Variations in the mode of scleral entry of the optic nerve give rise to anomalous congenital optic disc appearances, particularly tilted discs.
2. **The lamina cribrosa** consists of a series of plates of collagenous connective tissue which stretch across the posterior scleral foramen. It is perforated by 200–400 openings (pores) containing bundles of retinal nerve fibres. The largest pores are arranged in a vertical hourglass distribution at the superior and inferior poles, have thin connective tissue supports and contain large nerve fibres which are most vulnerable to glaucomatous damage. The superficial openings of the pores appear as grey dots deep within the optic cup. The appearance of the pores correlates with the severity of glaucomatous damage. If the damage is slight the pores are small and round, in moderately damaged eyes they are oval and in severe damage they are slit-like (see Fig. 9.37).

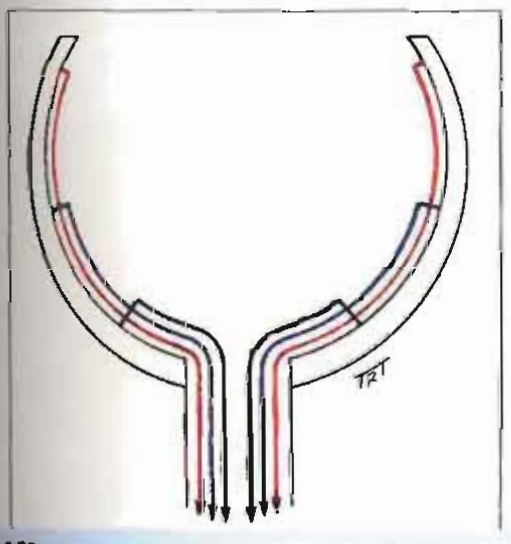

Fig. 9.25
Relative positions of retinal nerve fibres. (**Red**) peripheral; (**blue**) equatorial; (**black**) central

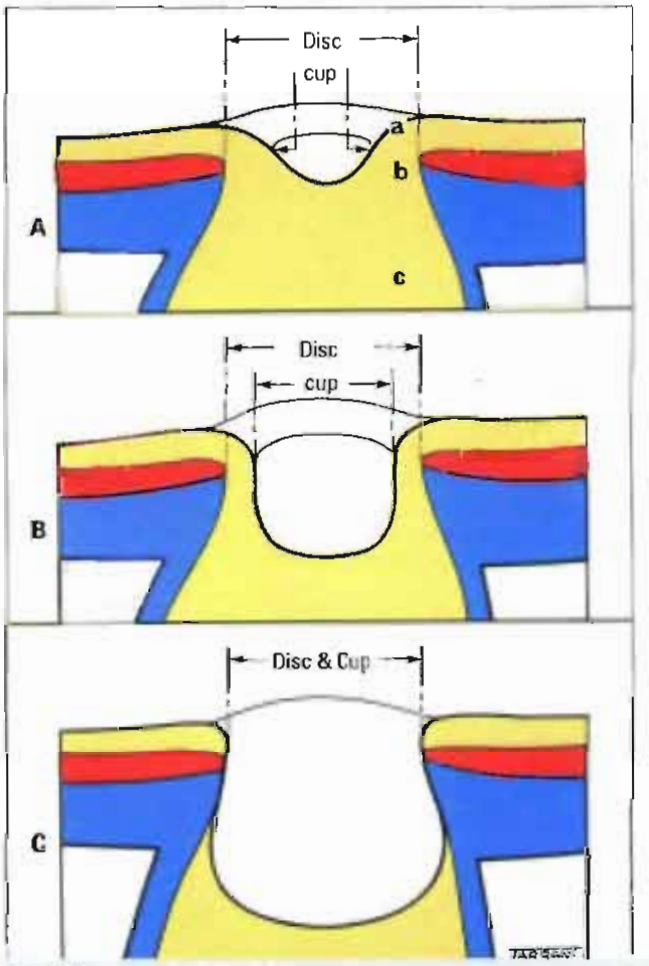

Fig. 9.26
Cross-section of the optic nerve head. (**A**) Small physiological cup: **a** = prelaminar layer, **b** = laminar layer, **c** = postlaminar layer; (**B**) large physiological cup; (**C**) total glaucomatous cupping

3. **The optic cup** is a pale depression in the centre of the optic nerve head which is not occupied by neural tissue. On direct ophthalmoscopy, it is best evaluated by observing the bending of the small blood vessels as they cross the disc, although on slit-lamp indirect ophthalmoscopy the actual borders of the cup may be appreciated three-dimensionally. The pallor of the cup results from exposure of the lamina cribrosa and lack of glial tissue in the centre of the disc. The size of the cup is related to the diameter of the disc. A small disc will have a small cup because the nerve fibres are crowded as they leave the eye, while a large disc will have a larger cup because the retinal nerve fibres are less crowded.
4. **Layers** (Fig. 9.26)
   a. ***The nerve fibre*** layer, the most superficial, is supported by astrocytes. It is readily visible ophthalmoscopically and is best visualized with red-free light.
   b. ***The prelaminar*** layer, consisting of retinal nerve fibres angling posteriorly from the plane of the retina, is visible only within the central cup (a in Fig. 9.26A).
   c. ***The laminar*** layer consists of the lamina cribrosa through which pass the retinal nerve fibres. The grey spots visible in the optic cup on ophthalmoscopy represent the anterior openings of the fenestrations in the lamina (b in Fig. 9.26A).
   d. ***The postlaminar*** layer consists of optic nerve posterior to the lamina cribrosa (c in Fig. 9.26A). The nerve fibres acquire myelin sheaths, due to which the diameter of the optic nerve doubles.

The normal optic nerve head

1. **The optic cup** may have three main appearances:
   - A dimple-like small central cup (Fig. 9.27).
   - A punched-out deep central cup (Fig. 9.28).
   - A cup with a sloping temporal wall (Fig. 9.29).
2. **The cup:disc ratio** indicates the diameter of the cup expressed as a fraction of the diameter of the disc and should be measured in both vertical and horizontal meridia. This ratio is genetically determined and is also dependent on the area of the disc. The neuroretinal rim (*see* below) occupies a relatively similar area in different eyes; large discs therefore have large cups with high cup–disc ratios. Most normal eyes have a vertical cup–disc ratio of 0.3 or less; only 2% have a ratio greater than 0.7. A ratio greater than 0.7 should therefore be regarded with suspicion although it may not necessarily be pathological. In any individual, asymmetry of 0.2 or more between the eyes should also be regarded with suspicion until glaucoma has been excluded.
3. **The neuroretinal rim** is the tissue between the outer edge of the cup and the disc margin. The normal rim has an orange or pink colour and shows a characteristic configuration. The inferior rim is the broadest, followed by superior, nasal and temporal (ISNT). A large physiological cup is due to a mismatch between the size of the scleral canal and the number of traversing nerve fibres which in health remains constant (*see* Fig. 9.26B). Pathological cupping is caused by an irreversible decrease in the number of nerve fibres, glial cells and blood vessels (*see* Fig. 9.26C).
4. **The blood vessels** from within the optic nerve enter the disc centrally and then course nasally following the edge of the cup. The central retinal artery is usually nasal to the vein.

Fig. 9.27
Normal disc with a small (dimple) cup

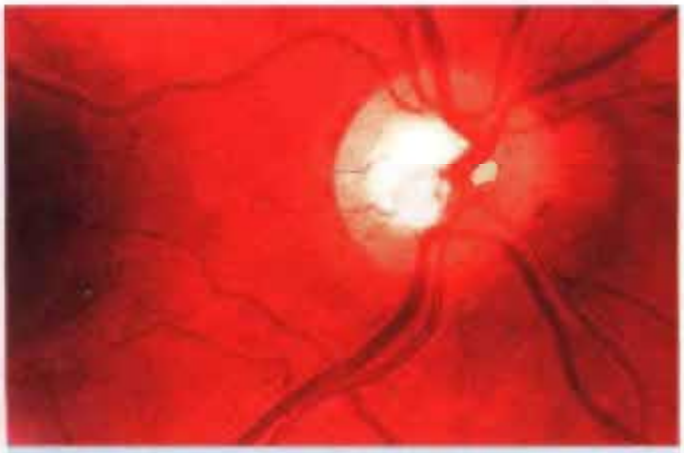

Fig. 9.28
Normal disc with a punched-out cup

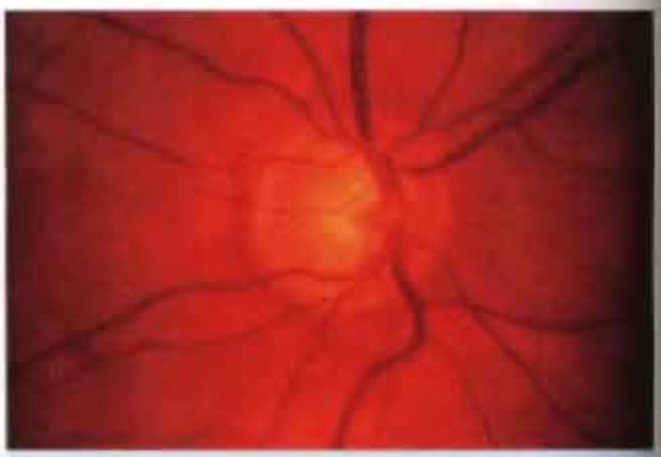

Fig. 9.29
Normal disc with a sloping temporal wall

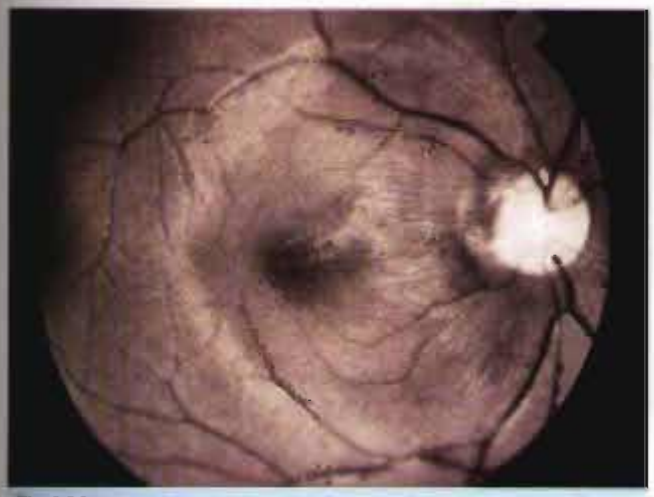

Fig. 9.30
Normal retinal nerve fibre layer, best seen with a green filter (Courtesy of J. Salmon)

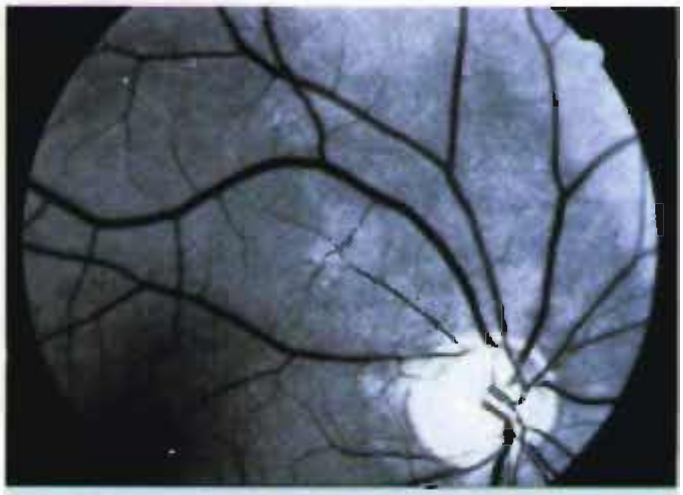

Fig. 9.32
Diffuse nerve fibre atrophy in advanced glaucoma. No striations are visible and the retinal blood vessels appear dark and sharply defined (Courtesy of J. Salmon)

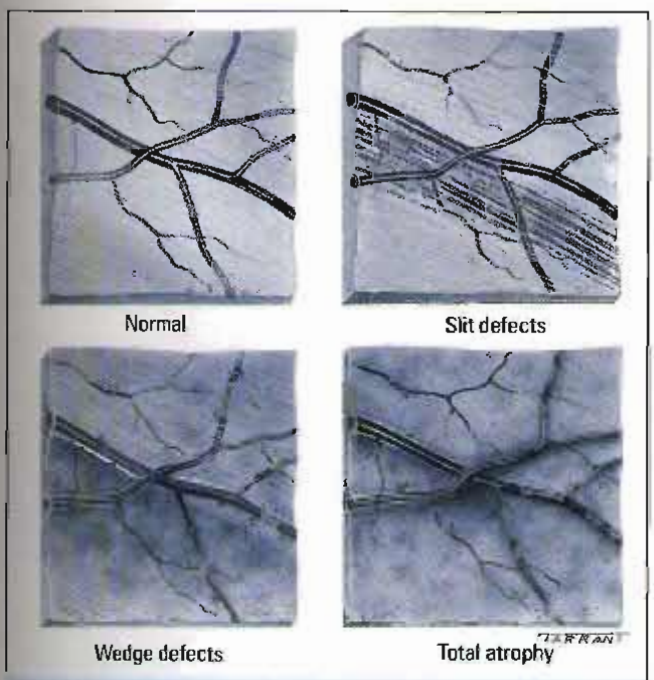

Fig. 9.31
Progression of glaucomatous retinal nerve fibre layer damage

Glaucomatous damage

Glaucomatous damage results in characteristic signs involving (a) *the retinal nerve fibre layer*, (b) *the optic nerve head* and (c) *the parapapillary area*.

Retinal nerve fibre damage

Figure 9.30 shows a normal retinal nerve fibre layer visualized with red-free light (a green filter). In glaucoma subtle retinal nerve fibre layer defects precede the development of detectable optic disc and visual field changes. Retinal nerve fibre dropout may be diffuse or localized. Early localized damage is characterized by slit or wedge-shaped defects in the retinal nerve fibre layer. As glaucomatous damage progresses the defects become larger; in end-stage glaucoma there is total atrophy of the nerve fibre layer characterized by complete baring of the larger retinal blood vessels, which run in this layer (Fig. 9.31). The atrophic area appears darker and mottled because of enhanced visualization of the retinal pigment epithelium (Fig. 9.32).

Optic disc damage

Optic disc damage is superimposed upon physiological cupping present prior to the onset of raised IOP. If an eye with a small cup develops glaucoma, the cup will increase in size, but during the early stages its dimensions may still be smaller than that of a large physiological cup. An estimation of cup size alone is therefore of limited value in the diagnosis of early glaucoma, unless it is found to be increasing. Glaucomatous cups are usually larger than physiological cups, although a large cup is not necessarily pathological. Assessment of the thickness, symmetry and colour of the neuroretinal rim is, however, more important. The spectrum of disc damage in glaucoma ranges from highly localized tissue loss with notching of the neuroretinal rim to diffuse concentric enlargement of the cup. Optic disc appearance is classified as follows:

1. **Type I** (focal ischaemic) disc is characterized by focal tissue loss at the superior and/or inferior poles (polar notching) and an otherwise relatively intact neuroretinal rim (Fig. 9.33). The notch is often associated with small areas of parapapillary atrophy or choroidal sclerosis (fundus tessellation). This type of disc tends to occur in older patients, particularly females, and is associated with localized field defects, with early threat to fixation. Particular attention should therefore be paid to neural tissue loss, in the vertical sectors of the cup.

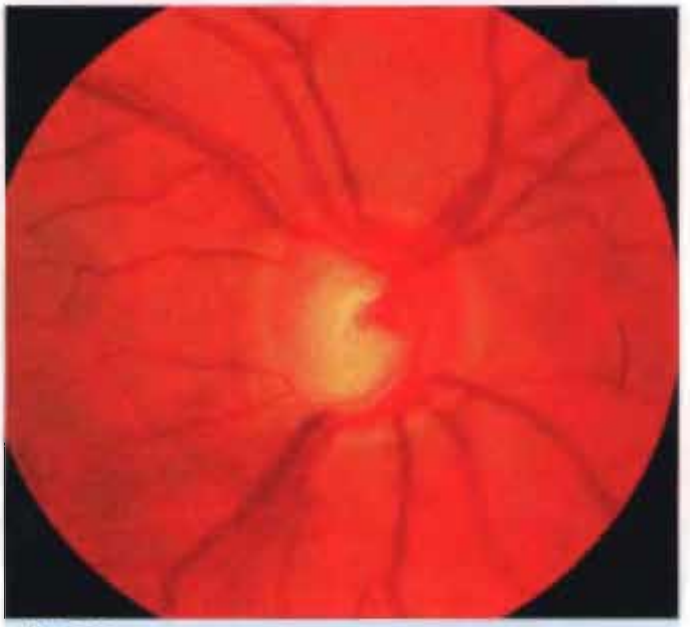

Fig. 9.33
Focal ischaemic glaucomatous damage

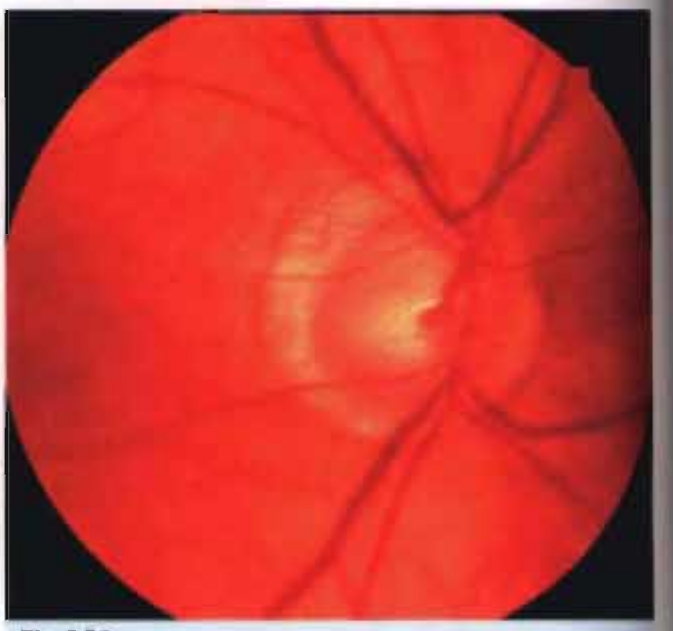

Fig. 9.35
Senile sclerotic glaucomatous disc

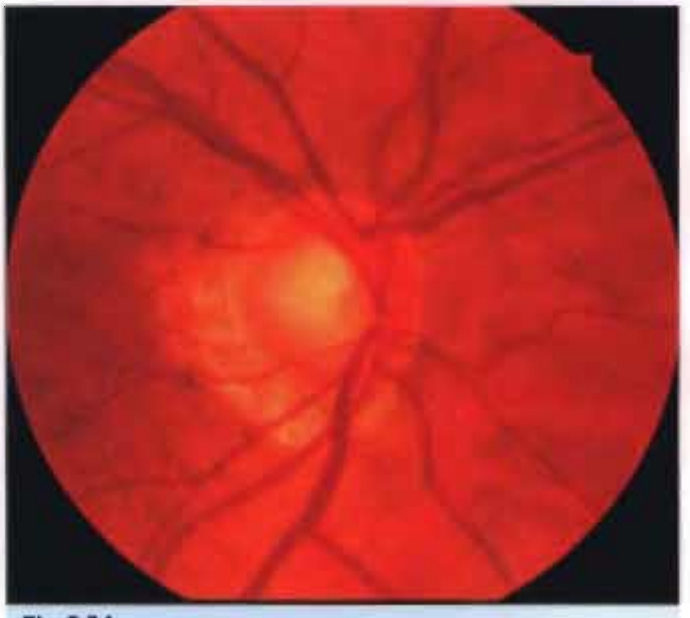

Fig. 9.34
Myopic glaucomatous disc

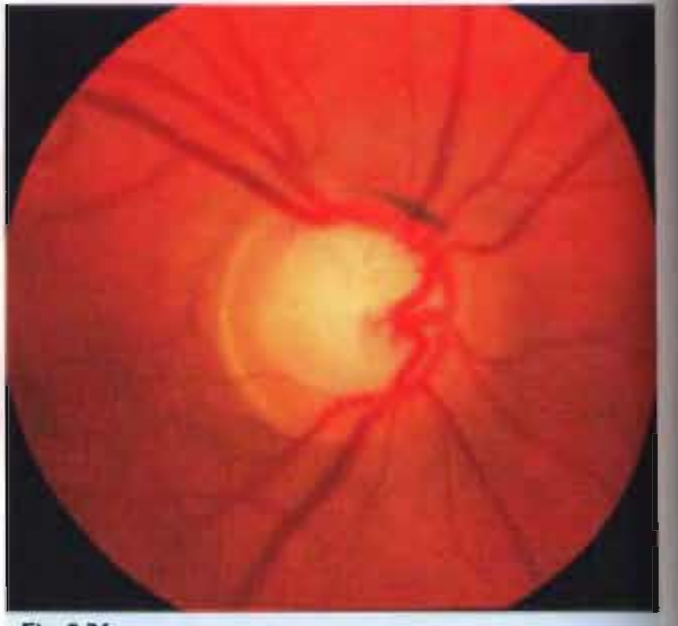

Fig. 9.36
Concentric glaucomatous enlargement

2. **Type 2** (myopic glaucomatous) disc is characterized by polar notching and a large temporal crescent in the absence of degenerative myopia (Fig. 9.34). It tends to occur in younger patients, particularly males, and is associated with localized visual field defects.
3. **Type 3** (senile sclerotic) disc is characterized by a shallow, saucerized cup and gently sloping neuroretinal rim, a 'moth-eaten appearance' and parapapillary atrophy or choroidal sclerosis surrounding the circumference of the nerve (Fig. 9.35). It tends to affect older patients and is associated with ischaemic heart disease and hypertension.
4. **Type 4** (concentric enlargement) disc is caused by diffuse loss of nerve fibres involving the entire cross-section of the optic nerve head, which results in a uniformly enlarged, round cup with no localized thinning of the neuroretinal rim (Fig. 9.36). This type of disc tends to occur in younger patients and is frequently associated with higher IOP and diffuse visual field loss. It may be very difficult to distinguish from a large physiological cup where the cup–disc diameter is still within normal limits. The best way to detect concentric enlargement of the cup is to compare it with a previous record.

Progression of glaucomatous damage

Figure 9.37 shows the progression of changes involving the optic disc and retinal nerve fibre layer.

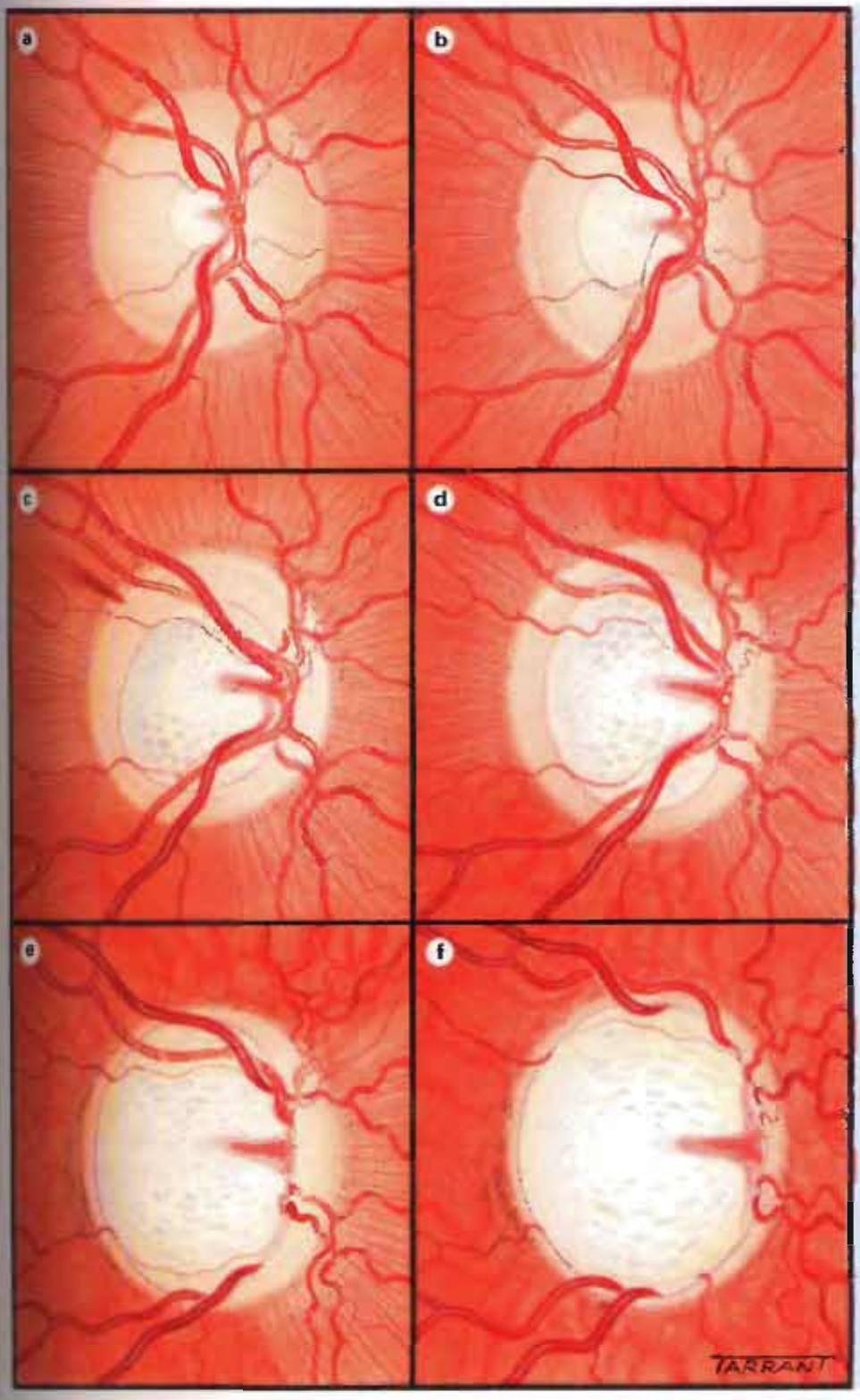

Fig. 9.37
Progression of glaucomatous optic nerve damage (see *text*)

- Figure 9.37a shows a normal disc with a small physiological cup and a cup–disc ratio of 0.2
- Figure 9.37b shows concentric enlargement and an increase in cup disc ratio to 0.5. The pores in the lamina cribrosa are small and round.
- Figure 9.37c shows inferotemporal expansion of the cup and a splinter-shaped haemorrhage on the disc margin, a frequent sign of imminent damage. There is corresponding loss of the inferior retinal nerve fibre layer and the pores in the inferior part of the cup are larger and oval.
- Figure 9.37d shows superior expansion of the cup so that it has become vertically oval. There is associated superior retinal nerve fibre loss and the pores in the superior lamina cribrosa are oval.

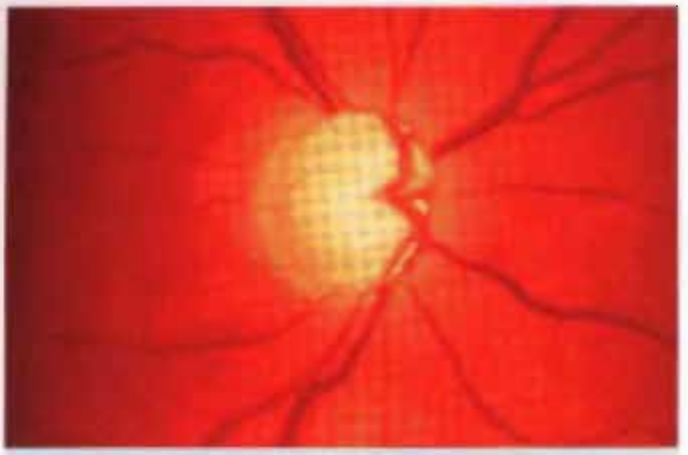

Fig. 9.38
End-stage glaucomatous cupping

- Figure 9.37e shows advanced cupping with total loss of superior, inferior and temporal disc tissue. There is associated retinal nerve fibre loss and the pores in the lamina cribrosa are slit-like. The progressive loss of nasal disc tissue has nasally displaced the central blood vessels emerging from the disc.
- Figures 9.37f and 9.38 show total cupping in which all neural disc tissue is destroyed and the optic nerve head appears white, deeply excavated with slit-like pores in the lamina cribrosa.

Parapapillary atrophy

Chorioretinal atrophy surrounding the optic nerve head is common in high myopia and may also occur in some healthy emmetropic eyes. There is, however, also a correlation between parapapillary atrophy and glaucoma. Atrophy surrounding the optic disc is conceptualized as consisting of two zones: an inner 'beta' zone, bordering the disc margin, which in turn is concentrically surrounded by an outer 'alpha' zone.

1. **Signs** (Fig. 9.39)
   a. ***The beta zone*** exhibits chorioretinal atrophy with visibility of the sclera and large choroidal blood vessels.
   b. ***The alpha zone*** displays variable irregular hyper- and hypopigmentation of the retinal pigment epithelium.
2. **Significance.** The alpha zone is larger in patients with POAG but its frequency is similar in glaucomatous and normal subjects. However, the beta zone is not only larger but also occurs more frequently in patients with POAG than in normal individuals. In unilateral POAG, the changes are more advanced in the affected eye. In ocular hypertension, the presence and size of parapapillary changes correlates with the subsequent development of optic disc and visual field damage. Approximately half of all ocular hypertensive eyes that convert to POAG exhibit progression of parapapillary atrophic changes.

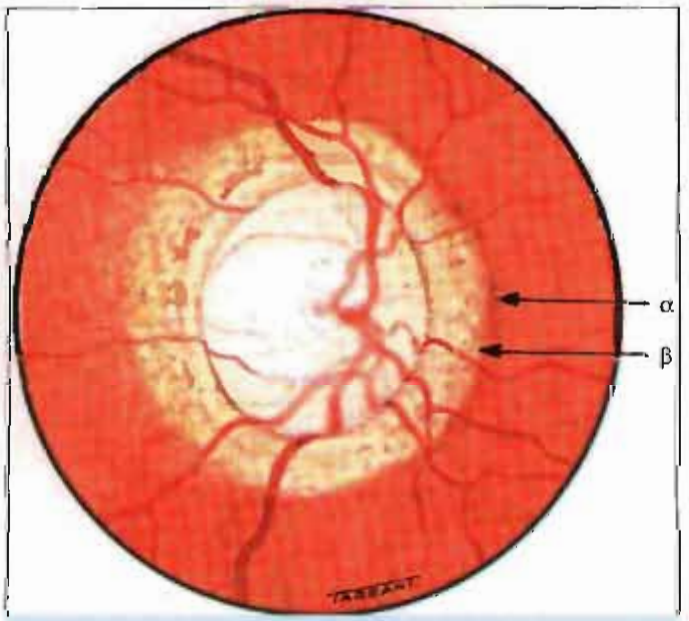

Fig. 9.39
Advanced glaucomatous cupping associated with parapapillary changes; a peripheral alpha zone and a central beta zone

Imaging techniques

A decade ago, fundus photography was the only method to document optic disc changes in glaucoma. Since then, sophisticated electronic devices have been developed with a view to offering an objective, quantitative, specific and reproducible method to diagnose glaucoma and monitor its progression. Although they provide information on optic nerve head topography and/or parapapillary retinal nerve fibre thickness, each device has specific advantages and limitations and is at different stages of development.

1. **The Heidelberg retinal tomograph** is a confocal laser scanning microscope designed for three-dimensional imaging of the posterior segment of the eye. Due to its ability to produce highly accurate and reproducible images, this sophisticated technology can most effectively be applied to the evaluation of the fundus at or around the optic nerve head. It does not, however, provide a direct measurement of retinal nerve fibre layer thickness.
2. **Optical coherence tomography** (OCT) provides high resolution cross-sectional images of the retina. Analogous to B scan ultrasonography which utilizes sound waves, OCT uses light from a superluminescent diode. Optical coherence tomographs can discriminate the cross-sectional morphological features of the fovea (*see* Fig. 13.71) and optic disc, the layered structure of the retina, and normal anatomical variations in retinal and retinal nerve fibre layer thickness with a resolution of 10 μm. In glaucoma, retinal nerve fibre thickness is measured at standardized locations around the optic nerve head. Additional radial scans through the optic nerve head afford the evaluation of cupping and juxtapapillary retinal nerve fibre layer thickness. A large pupil and clear media are required for accurate measurements.

3. **Scanning laser polarimetry** (the Nerve Fibre Analyser) is based on the assumption that the retinal nerve fibre layer has birefringent properties. The change in polarization, called retardation, can be quantified by determining the phase shift between polarization of light returning from the eye with that of the illuminating laser beam. The degree of retardation is linearly related to retinal nerve fibre thickness.

> **NB:** Currently, these techniques are still largely in the experimental stages. Conventional disc photography still remains the examination of choice in routine glaucoma practice.

Perimetry

Introduction

Definitions

1. **The visual field** may be described as an island of vision surrounded by a sea of darkness (Fig. 9.40). It is not a flat plane but a three-dimensional structure akin to a hill of vision. The outer aspect of the visual field extends approximately 50° superiorly, 60° nasally, 70° inferiorly and 90° temporally. Visual acuity is sharpest at the very top of the hill (i.e. the fovea) and then declines progressively towards the periphery, the nasal slope being steeper than the temporal. The blind spot is located temporally between 10° and 20°.
2. **An isopter**. As the size and luminance of a target are decreased, the area within which it can be perceived becomes smaller, so that a series of ever-diminishing circles called isopters is formed. Isopters therefore resemble the contour lines on a map which enclose an area within which a target of a given size is visible. An erosion of the 'coastline' of the island will therefore cause an indentation of all isopters in the affected area.
3. **A scotoma** is an area of visual loss, surrounded by vision.
   a. ***An absolute*** scotoma represents total loss of vision. Even the largest and brightest target cannot be perceived.
   b. ***A relative*** scotoma is an area of partial visual loss within which brighter or larger targets can be seen and smaller or dimmer ones cannot. A scotoma may have sloping edges so that an absolute scotoma is surrounded by a relative scotoma.
4. **Luminance** is the intensity or 'brightness' of a light stimulus, measured in apostilb (asb). A decibel (dB) is a non-specific unit of luminance based on a logarithmic scale (one-tenth of a log unit).
5. **Differential light sensitivity** represents the degree by which the luminance of a target requires to exceed background luminance in order to be perceived by the eye. The visual field is therefore a three-dimensional representation of differential light sensitivity at different points.
6. **Visible threshold** is the luminance of a given stimulus (measured in asb or dB) at which it is perceived 50% of the time when presented statically. The threshold is determined by increasing the intensity of the stimulus by 0.1 log unit steps. The human eye needs about a 10% change in brightness to discern a difference between light stimuli. For example, at a background illumination of 0.1 asb, the eye can detect a light stimulus that is 0.01 asb brighter, while at a background illumination of 1000 asb the eye requires a light that is 100 asb brighter to detect a difference. The threshold sensitivity (differential light sensitivity) is highest at the fovea and decreases progressively towards the periphery. After the age of 20 years the sensitivity decreases by 1 dB per 10 years. For example, at age 20 years the sensitivity at the fovea is 35 dB, at age 30 years it will be 34 dB, and at age 70 years it will be 30 dB.

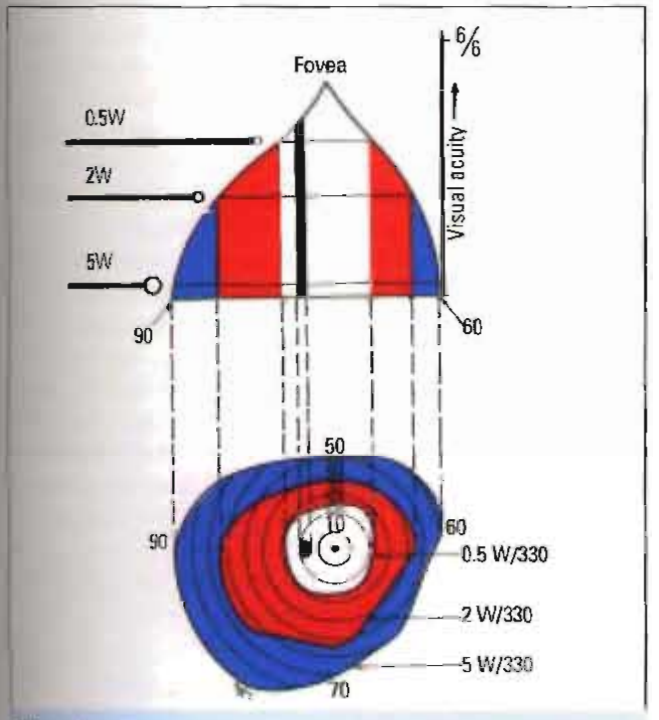

Fig. 9.40
Visual field and isopters. 0.5 W/330 = 0.5 mm white target at 0.33 metre; 2 W/330 = 2 mm white target at 0.33 metre; 5 W/330 = 5 mm white target at 0.33 metre

Types of perimetry

Perimetry involves evaluation of the visual field. Because of the subjective variability of patients' responses, efforts have been made to standardize the many aspects of testing in an endeavour to eliminate as many variables as possible. Nevertheless, when interpreting a visual field defect, it is important to take into account the patient's reliability.

1. **Kinetic** perimetry is a two-dimensional assessment of the boundary of the hill of vision. It involves the presentation of a moving stimulus of known luminance or intensity from a non-seeing area to a seeing area until it is

perceived. The stimulus is moved at a steady speed along various meridia (clock hours) and the point of perception is recorded on a chart. By joining these points along different meridians an isopter is plotted for that stimulus intensity. Using stimuli of different intensities a contour map of the visual field with several different isopters can be plotted. Kinetic perimetry can be performed by simple confrontation, the tangent screen, the Lister perimeter and the Goldmann perimeter.

2. **Static** perimetry is a more difficult concept to perceive but once grasped forms the basis of modern glaucoma assessment. It is a three-dimensional assessment of the height (differential light sensitivity) of a predetermined area of the hill of vision. Static perimetry involves the presentation of non-moving stimuli of varying luminance in the same position to obtain a vertical boundary of the visual field.
   a. ***Suprathreshold*** perimetry is used mainly for screening. It involves the presentation of visual stimuli at luminance levels above expected normal threshold values (suprathreshold) in various locations in the visual field. Detected targets indicate grossly normal visual function, whereas missed targets reflect areas of decreased visual sensitivity. Missed points can later be quantified (i.e. threshold measured). Selecting an appropriate suprathreshold intensity is important; if too high, subtle early defects may be missed, and if too low, close to threshold, a large number of normal individuals will miss stimuli.
   b. ***Threshold*** perimetry is used for detailed assessment of the hill of vision by plotting the threshold luminance value in various locations in the visual field and comparing the results with age-matched 'normal' values. In Humphrey perimetry (*see* below), the intensity of a stimulus is increased by 4 dB steps until threshold is crossed. Threshold is then redetermined by decreasing the intensity by 2 dB steps. Because threshold perimetry represents quantitative assessment it is the most accurate method of monitoring glaucomatous visual field defects.

Printouts

Printouts of a test contain geographic (i.e. grey scale) and numerical results. The latter generally includes the raw data (i.e. sensitivity in dB at each test location), the difference between the patient's results and that expected of a patient of similar age, and summary data (visual field indices). These indices include an assessment of diffuse field loss, localized defects and patient reliability.

Sources of error

The skill of the perimetrist in setting up the test, explaining the procedure to the patient, reassuring the patient and monitoring performance is fundamental to obtaining an accurate field. However, errors may still occur as a result of one or more of the following factors:

1. **Miosis** decreases threshold sensitivity in the peripheral field and increases variability in the central field in both normal and glaucomatous eyes. Pupils less than 3 mm in diameter should therefore be dilated prior to perimetry.
2. **Lens opacities** have a profound effect on the visual field, which is exaggerated by miosis.
3. **Uncorrected refractive error** can cause a significant decrease of central sensitivity. If a hypermetropic patient who usually wears contact lenses is tested wearing spectacles this will have the effect of magnifying and enlarging any scotomas as compared to contact lenses.
4. **Spectacles** can cause rim scotomas if small-aperture lenses are used or if incorrectly dispensed.
5. **Ptosis**, even if mild, can result in suppression of the superior visual field.
6. **Inadequate retinal adaptation** may also lead to error if perimetry is performed soon after ophthalmoscopy.

Humphrey perimetry

The Humphrey perimeter consists of a white bowl with a background luminance of 31.5 asb, the lower end of photopic illumination. Target luminance can be varied between 0.08 asb and 10,000 asb brighter than background, which equates to a decibel range of 51–0. Variation in stimulus intensity is achieved by altering target size or luminance. Stimulus size is set prior to the test; only luminance is altered while the test is in progress in order to determine the threshold level for each point tested in the visual field.

Programs

The Humphrey has a range of suprathreshold and full threshold strategies (e.g. 30–1, 24–2). The number before the dash (24– or 30–) indicates the area of the tested field, in degrees from fixation. The 24° strategy tests 54 points and the 30° tests 76 points. The number after the dash (–1 or –2) describes the pattern of the points tested. The –2 strategy involves a grid of test points spaced 6° apart, offset from the vertical and horizontal meridia whereas the –1 includes points along the vertical and horizontal meridia. The most commonly performed central full threshold strategy is 24–2. Initially four points are tested to determine threshold levels, which are then used as a starting level for neighbouring points and so on until the entire field has been tested. Points where the anticipated response is outside 5 dB of that expected are retested a second time; the second response is indicated in brackets on the final printout. Different programs provided by the manufacturer include STATPAC, EASTPAC and SITA (Swedish Interactive Threshold Algorithm). The latter is the fastest and perhaps the most user-friendly. It also has the advantage of reacting to the patient's responses and timing to customize the determination of thresholds and the pacing of the test.

Reliability indices

Reliability indices (Fig. 9.41a) reflect the extent to which the patient's results are reliable and should be analysed first. If grossly unreliable, further evaluation of a visual field printout is pointless.

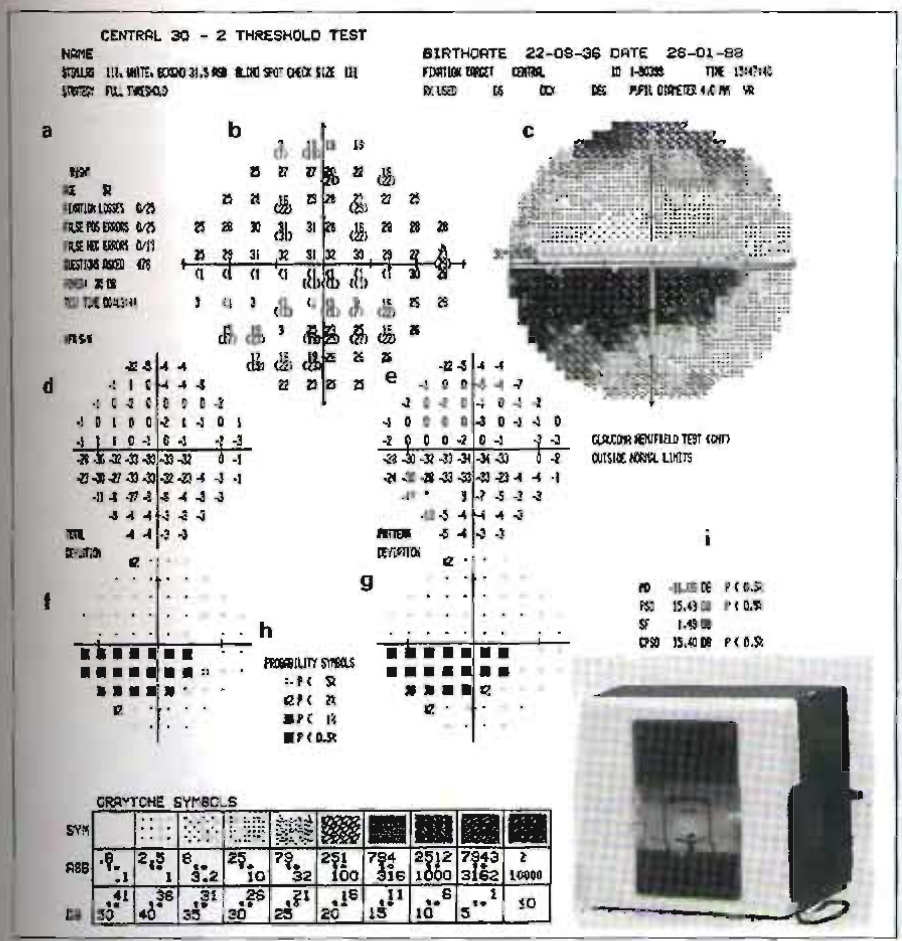

Fig. 9.41
Humphrey perimetric printouts (see text)

1. **Fixation losses** indicate steadiness of gaze during the test. They are detected by presenting stimuli in the physiological blind spot. If the patient responds, a fixation loss is recorded. The lower the number of losses the more reliable the test. A high fixation loss score may occur if the instrument has incorrectly plotted the blind spot.
2. **False positives** are detected when a stimulus is accompanied by a sound. If the sound alone is presented (without an accompanying light stimulus) and the patient still responds, a false positive is recorded. A high false positive score suggests a 'trigger-happy' patient and is the most sensitive indicator of an unreliable field.
3. **False negatives** are detected by presenting a stimulus much brighter than threshold at a location where sensitivity has already been recorded. If the patient fails to respond a false negative is recorded. A high false negative score indicates inattention. It may also be due to short-term fluctuation that is associated with glaucoma, and may be an indicator of disease severity rather than patient unreliability.

> **NB:** In patients who constantly fail to achieve good reliability indices it may be useful to switch to a suprathreshold strategy.

Displays

1. **The greyscale** (Fig. 9.41c), in which decreasing sensitivity is represented by darker tones, is the simplest to interpret. The scale at the bottom of the chart shows corresponding values of the greytone symbols in abs and dB. Each change in greyscale tone is equivalent to 5 dB change in threshold.
2. **The numerical** display (Fig. 9.41b) gives the threshold (dB) for all points checked. The figures in brackets indicate threshold at the same point checked a second time, if on initial testing it was at least 5 dB less sensitive than expected.
3. **The total deviation** represents the deviation of the patient's result from that of age-matched controls. The upper numerical display (Fig. 9.41d) illustrates the differences in dB and the lower display (Fig. 9.41f) exhibits these differences as grey symbols.
4. **Pattern deviation** (Figs 9.41e and g) is similar to total deviation except that it is adjusted for any generalized depression in the overall field which might be caused by other factors such as lens opacities or miosis.

Probability values (p) (Fig. 9.41h) indicating the significance of the defects are shown as <5%, <2%, <1% and <0.5%. The lower the p value the greater its clinical significance and the lesser the likelihood of the defect having occurred 'by chance'.

Global indices

Global indices (Fig. 9.41i) summarize the results in a single number and are principally used to monitor progression of glaucomatous damage rather than for initial diagnosis.

1. **Mean deviation** (MD) (elevation or depression) is a measure of the overall field loss.
2. **Pattern standard deviation** (PSD) is a measure of focal loss or variability within the field taking into account any generalized depression in the hill of vision. An increased PSD is therefore a more specific indicator of glaucomatous damage than MD.
3. **Short-term fluctuation** (SF) is an indication of the consistency of responses. It is assessed by measuring threshold twice at ten pre-selected points and is calculated on the difference between the first and second measurements.
4. **Corrected pattern standard deviation** (CPSD) is a measure of variability within the field after correcting for short-term fluctuation (intra-test variability).

Minimal criteria for glaucomatous damage

One of the following:

1. Glaucoma hemifield test outside normal limits on at least two consecutive occasions. This provides information concerning differences between the superior and inferior halves of the visual field by evaluating threshold at mirror image points above and below the horizontal meridian.
2. A cluster of three or more non-edge points in a location typical for glaucoma, all of which are depressed on PSD at a $p < 5\%$ level and one of which is depressed at a $p < 1\%$ level, on two consecutive occasions.
3. A CPSD that occurs in less than 5% of normal individuals on two consecutive fields.

NB: Visual fields should not be interpreted in isolation but in conjunction with clinical findings such as the level of IOP, and the appearance of the optic disc and retinal nerve fibre layer.

Glaucomatous damage

Characteristic defects

1. The earliest changes suggestive of glaucoma consist of increased variability of responses in areas that subsequently develop defects. Alternatively there may be slight asymmetry between the two eyes.

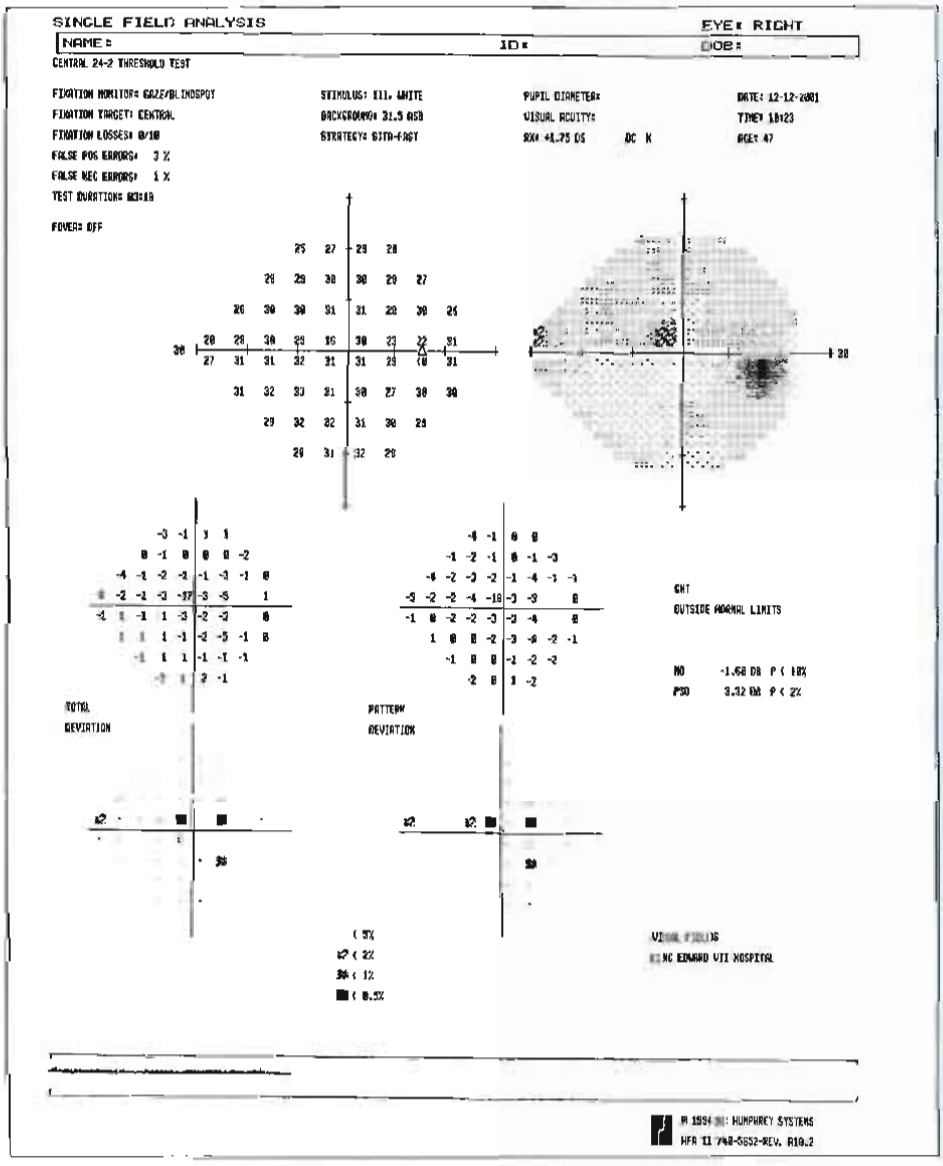

Fig. 9.42
Paracentral scotoma

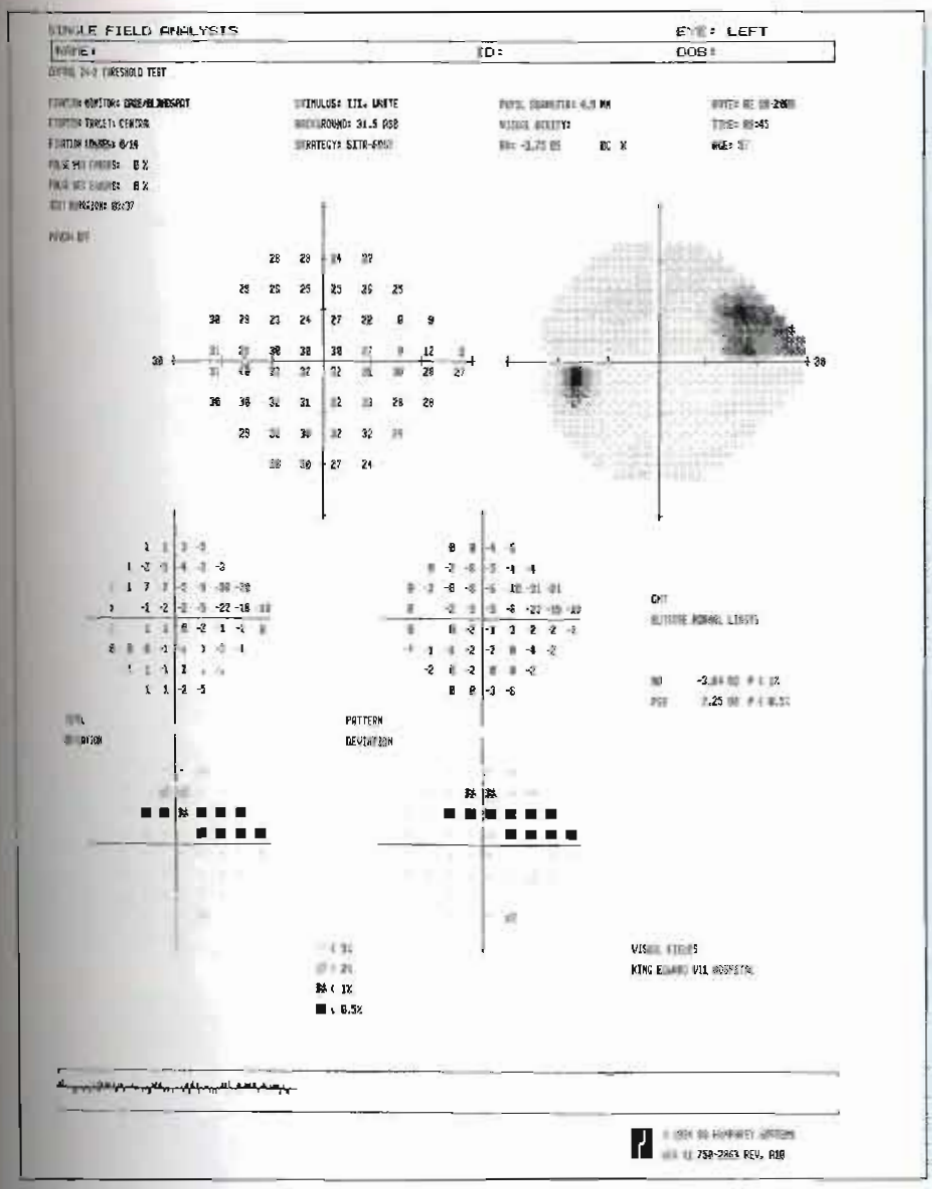

Fig. 9.43
Nasal (Roenne) step

2. Paracentral, small, relatively steep depressions, most commonly superonasally (Fig. 9.42), constitute approximately 70% of all early glaucomatous field defects. Since the defects respect the distribution of the retinal nerve fibre layer they terminate at the horizontal midline. Defects above and below the horizontal therefore are not aligned with each other.
3. A nasal (Roenne) step represents a difference in sensitivity above and below the horizontal midline in the nasal field (Fig. 9.43). It is a common finding usually associated with other defects. A temporal wedge is less common but has similar implications.
4. Arcuate-shaped defects develop as a result of coalescence of paracentral scotomas. They typically develop between 10° and 20° of fixation in areas that constitute downward, or more commonly, upward extensions from the blind spot around fixation (Bjerrum area). With time, they tend to elongate circumferentially along the distribution of arcuate nerve fibres (Seidel scotoma) and may eventually connect with the blind spot (arcuate scotoma), reaching to within 5° of fixation nasally (Fig. 9.44).
5. Enlargement and deepening of existing scotomas (Fig. 9.45) and development of fresh scotomas (Fig. 9.46).
6. Peripheral breakthrough due to damage to adjacent fibres.
7. A ring scotoma develops when arcuate defects in upper and lower halves of the visual field join. Misalignment between the two often preserves the nasal step (Fig. 9.47).
8. End-stage changes are characterized by a small island of central vision and an accompanying temporal island. The temporal island is usually extinguished before the central.

NB: Progression of damage can be identified not only by increase in the number of scotomas and/or an increase in depth of existing scotomas but also by deterioration of total and pattern deviations and global indices (Fig. 9.48).

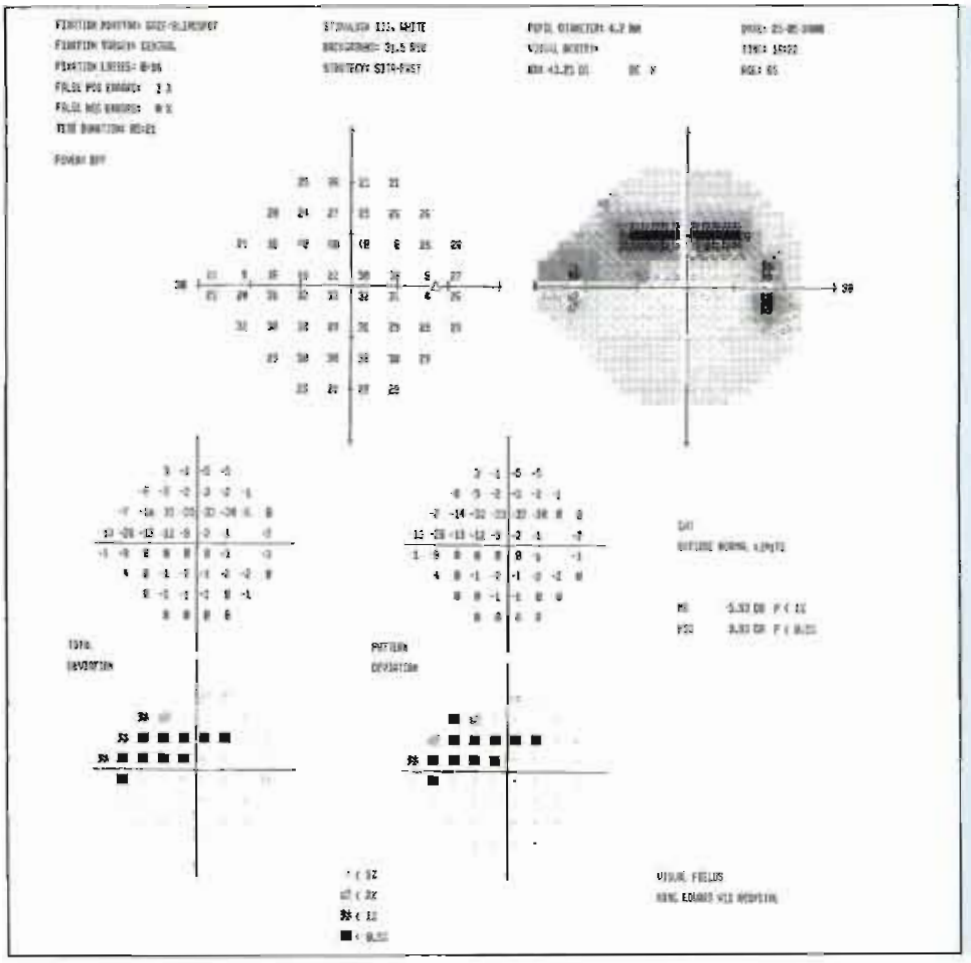

Fig. 9.44
Arcuate scotoma

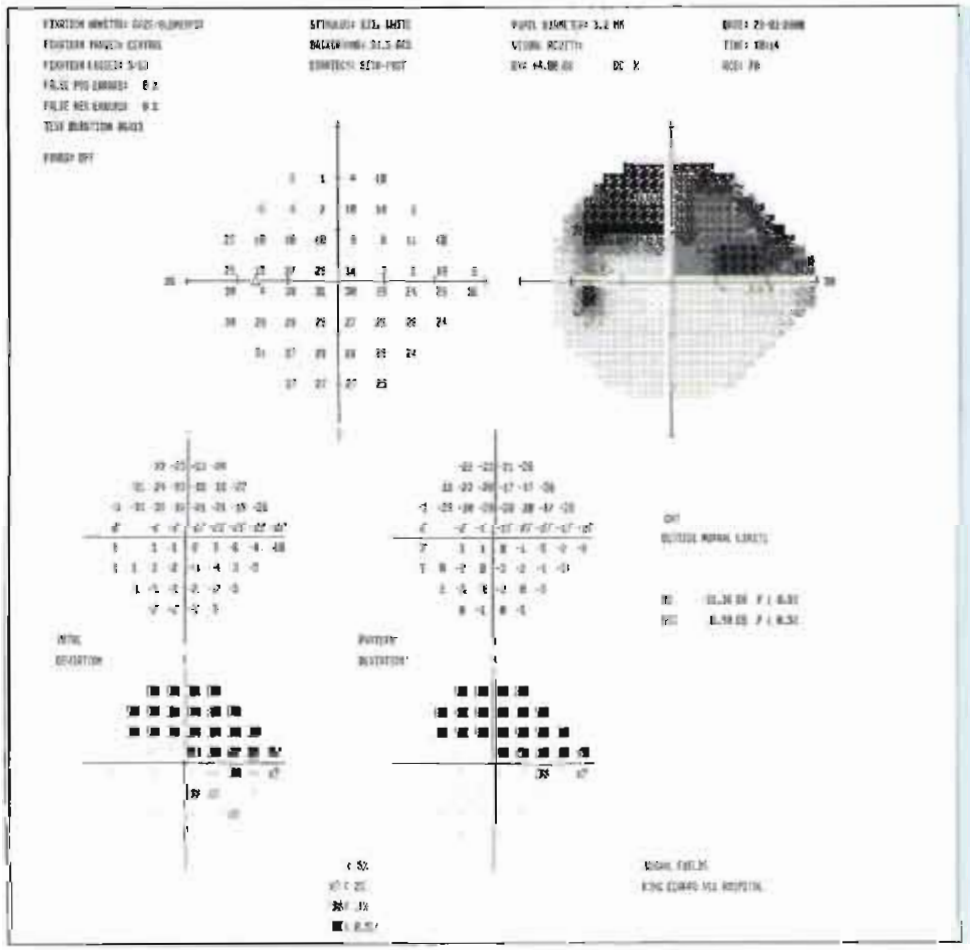

Fig. 9.45
Advanced superior arcuate visual field defect

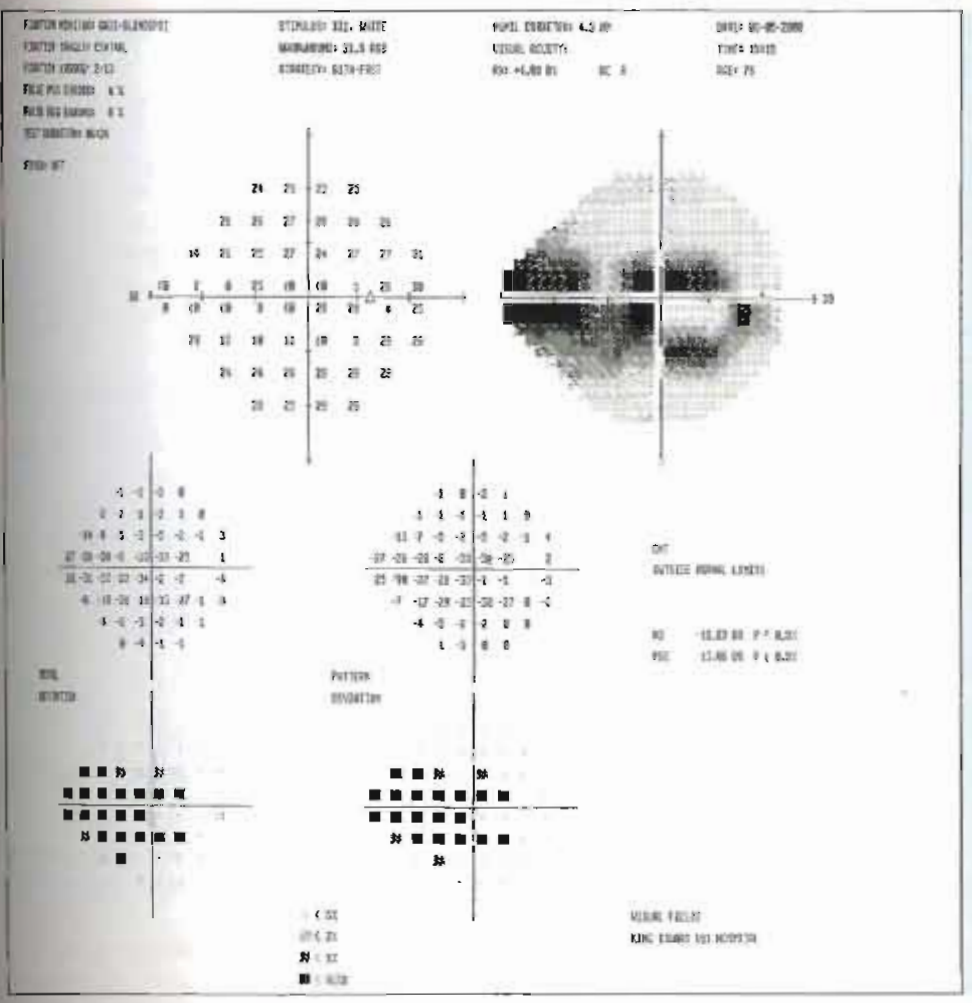

Fig. 9.46
Inferior and superior arcuate visual field defects

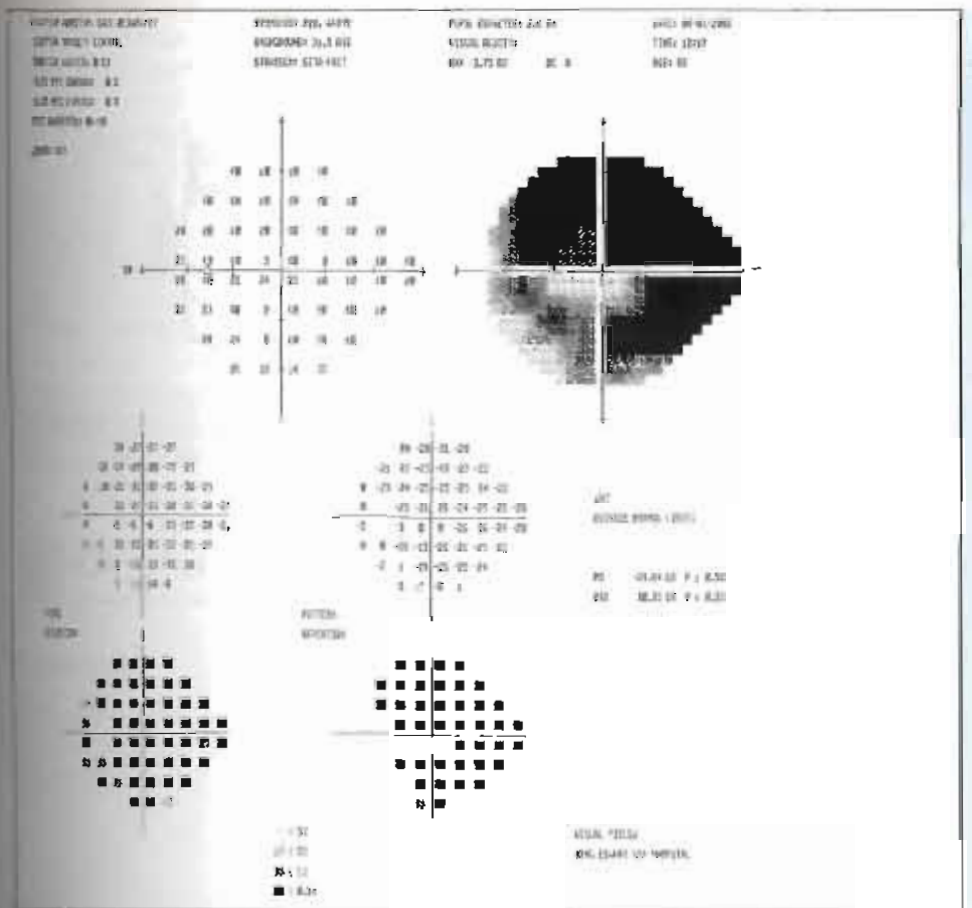

Fig. 9.47
Advanced visual field loss

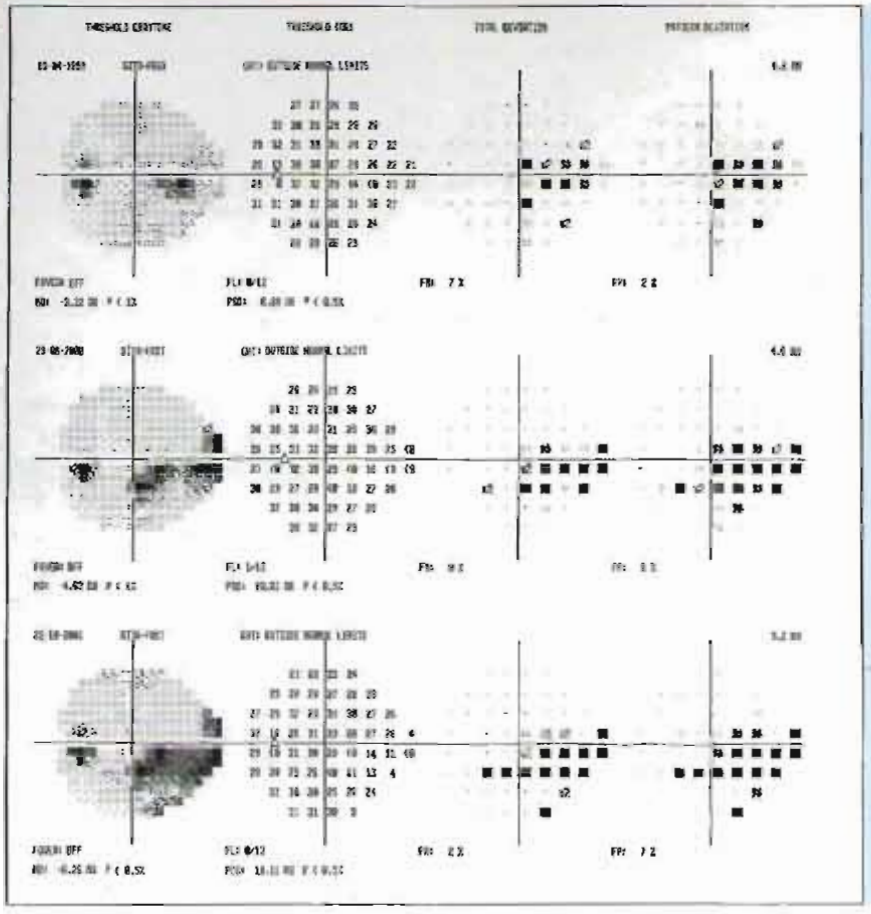

Fig. 9.48
Progression of visual field defects over three years

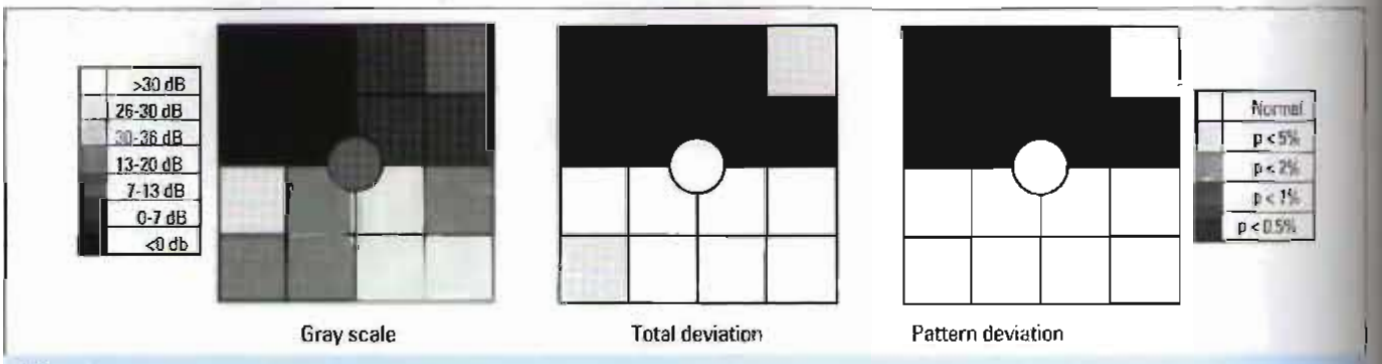

Fig. 9.49
Printout of frequency doubling perimetry showing moderate visual field loss

Other psychophysiological tests

It has been estimated that focal loss of at least 20% of retinal ganglion cells is required before glaucomatous field defects can be detected using conventional perimetry. Learning effects are often found whereby field defects disappear on repeated testing. Genuine early glaucomatous defects may also be transient and disappear with lowering of IOP. Alternative methods of detecting early defects are therefore being developed.

Physiological principles

Ganglion (M) cells with relatively large-diameter axons comprise 25% of the ganglion cell population. They are particularly susceptible to glaucomatous damage and appear to be preferentially lost in early glaucoma. A loss of a small number of these cells therefore has a considerable effect on visual function. Psychophysiological tests designed to target visual function provided by this magnocellular pathway in the detection of early glaucoma have been devised.

Perimetric tests

1. **Frequency doubling perimetry** is a simple and rapid test which shows considerable promise. It is based on the frequency doubling illusion which is produced when a low spatial frequency sinusoidal grating undergoes high temporal frequency counter phase flicker. The rapid alternation in which the light bars become dark and vice versa, produces the illusion of the grating having doubled its frequency. The perimeter is a tabletop portable instrument which can be used under normal room lighting and requires no patching, since the viewing canopy automatically covers the eye not being tested. The stimuli are presented in 17 or 19 sectors in the central 20° or 30° depending on the program used, screening or full threshold. The test results are displayed and printed together with reliability indices, probabilities, mean deviation and pattern standard deviation (Fig. 9.49).
2. **Short wave automated perimetry** (SWAP) reflects the function of P (parvocellular) cells by displaying a blue stimulus on a yellow background. It is a good method of detecting early defects in young patients but lens-induced artefacts have limited its use in elderly patients.

Ocular hypertension

Introduction

The term 'ocular hypertension' is used when the IOP is found to be >21 mmHg on two consecutive occasions, in the absence of detectable glaucomatous damage. In population based studies, the mean IOP is 16 mmHg: two standard deviations on either side of this gives a 'normal' IOP range from 11 to 21 mmHg. The distribution is Gaussian with the curve skewed to the right (Fig. 9.50). In the elderly the mean IOP is higher, particularly in women, and the standard deviation greater than in younger individuals. This means that 'normal' IOP in elderly women may range up to 24 mmHg and not 21 mmHg.

Risk for developing glaucoma

Although 4–7% of the population over the age of 40 years have IOPs >21 mmHg, only 1% of individuals with ocular hypertension will develop glaucoma each year. The risk of damage increases as the IOP rises. The prevalence of primary open-angle glaucoma (POAG) in relation to screening IOP is shown in Table 9.1. There is no infallible way of predicting who will eventually develop glaucoma. Structural changes in the retinal nerve fibre layer and the optic nerve head precede changes in visual function (pre-perimetric glaucoma). It may therefore take up to several years before damage can be detected by conventional perimetry, which necessitates loss of 20% of the ganglion cell population.

Management

Most patients with ocular hypertension do not require treatment and only those at high risk should be treated in

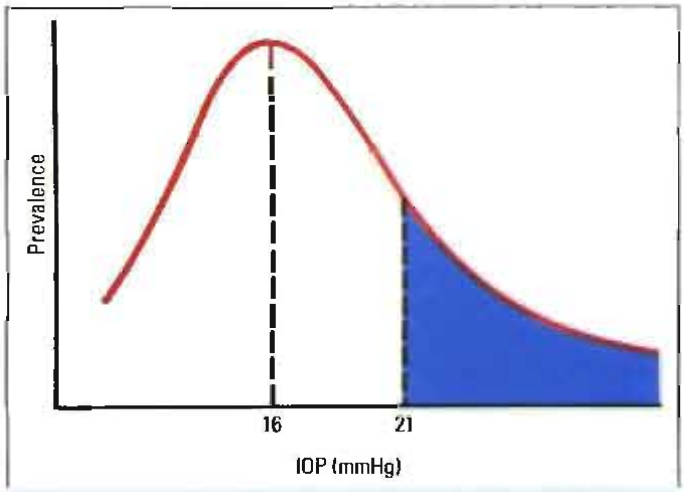

Fig. 9.50
Distribution of intraocular pressure in the general population

Table 9.1 Relationship between prevalence of POAG and IOP

IOP (mmHg)	*Prevalence of POAG (%)*
16–21	1.5
22–29	8
30 or over	25

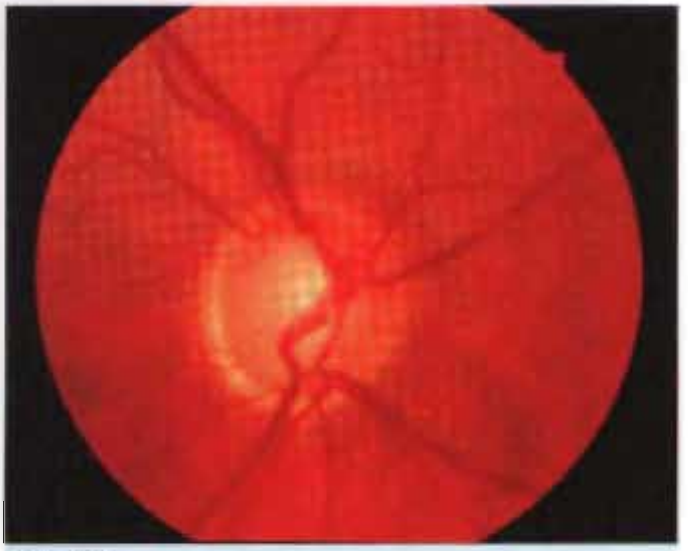

Fig. 9.51
Vertical cup–disc ratio over 0.7

order to delay or prevent the development of POAG. It should be remembered that once treatment is instituted, it is continued throughout the patient's lifetime and may have significant side effects. Therapeutic decisions in individual patients are based on a combination of risk factors as follows:

1. **High risk factors**
   - Retinal nerve fibre layer defects.
   - Parapapillary changes.
   - IOP 30 mmHg or more.
   - IOP 26 mmHg or more and central corneal thickness < 555 μm.
   - Vertical cup–disc ratio 0.4 or more and corneal thickness < 588 μm.

Most patients with high risk factors should be treated because treatment is effective in delaying or preventing the development of POAG in a significant proportion of cases. A change of IOP is more important than a specific level and it is reasonable to aim for a 20% reduction of IOP.

2. **Moderate risk factors**
   - IOP of 24–29 mmHg without nerve fibre layer defects.
   - Vertical cup–disc ratio > 0.3 (Fig. 9.51) and central corneal thickness > 588 μm.
   - Family history of POAG in a first degree relative.
   - High myopia.

In these patients annual examination of the optic discs and perimetry is appropriate. Treatment is withheld until damage is documented.

Primary open-angle glaucoma

Introduction

Primary open-angle glaucoma (POAG), also referred to as chronic simple glaucoma, is a generally bilateral, but not always symmetrical disease, characterized by:

- Adult onset.
- An IOP > 21 mmHg at some point in the course of the disease.
- An open angle of normal appearance.
- Glaucomatous optic nerve head damage.
- Visual field loss.

Despite this definition it should be emphasized that approximately 16% of all patients with otherwise characteristic POAG will have IOPs consistently below 22 mmHg. Moreover, the majority of individuals with IOP > 21 mmHg do not have glaucoma. POAG is the most prevalent type of glaucoma, affecting approximately 1 in 100 of the general population over the age of 40 years. It affects both sexes equally and is responsible for about 12% of all cases of blind registration in the UK and the USA.

Risk factors and associations

1. **Age**. POAG is more common in older individuals, most cases presenting after the age of 65 years. It is unusual for this diagnosis to be made before the age of 40 years.
2. **Race**. POAG is significantly more common, develops earlier, and is more severe, in black people than in white.
3. **Family history and inheritance**. POAG is frequently inherited, probably in a multifactorial manner. The responsible genes are thought to show incomplete penetrance and variable expressivity. Intraocular pressure, facility of aqueous outflow and optic disc size are also genetically determined. First-degree relatives of patients with POAG are at increased risk of developing POAG; however, estimates of exact risk are lacking because the disease develops in older individuals and long-term follow-up is required for accurate figures. However, an approximate risk to siblings of 10% and to offspring of 4%, has been suggested.
4. **Myopia** is associated with an increased incidence of POAG and myopic eyes are also more susceptible to pressure-induced damage.
5. **Retinal disease**. Central retinal vein occlusion is associated with an increased incidence of POAG. Approximately 5% of patients with rhegmatogenous retinal detachment and 3% of those with retinitis pigmentosa have associated POAG.

Steroid responsiveness

The normal population can be divided into three groups on the basis of their IOP response to a 6-week course of topical betamethasone.

1. **High responders** exhibit a marked elevation of IOP (>30 mmHg).
2. **Moderate responders** display a moderate elevation of IOP (22–30 mmHg).
3. **Non-responders** manifest virtually no change in IOP.

The incidence of steroid responders is shown in Table 9.2. Topical steroids should be used with caution in these individuals. However, in a high or intermediate steroid responder, the 'strong' steroids (dexamethasone, betamethasone and prednisolone) are equipotent in their ability to raise IOP, while fluorometholone has a lesser propensity to raise IOP: fluorometholone raises IOP half as much as betamethasone.

Table 9.2 Incidence of steroid responsiveness

	High (%)	*Moderate (%)*	*Non (%)*
General population	5	35	60
Patients with POAG	90	10	0
Siblings of patients with POAG	30	50	20
Offspring of patients with POAG	25	70	5

NB: Systemic steroids are much less prone to cause elevation of IOP, but more likely to induce cataract.

Genetics

1. **Steroid responsiveness** is of great interest in the genetics of POAG. A mutation of the *MYOC* gene is strongly associated with a subset of juvenile open-angle glaucoma, and is present in about 4% of adults with POAG. The gene was previously named *TIGR* (trabecular induced glucocorticoid response). It resides in the *GLC1A* region of the long arm of chromosome 1 and codes for a protein called myocilin. The administration of steroids in steroid responders induces gene expression and the production of excessive quantities of myocilin. However, the exact role of myocilin in the pathogenesis of steroid-induced elevation of IOP is currently unclear.
2. **Other aspects.** All gene loci associated with POAG have a prefix GLC1, with a suffix letter indicating the temporal order in which the gene is identified. Genes that have so far been identified in certain families with POAG lie on chromosome 2 (*GLC1B*), chromosome 3 (*GLC1C*), chromosome 8 (*GLC1D*), chromosome 10 (*GLC1E*) and chromosome 7 (*GLC1F*).

Pathogenesis of glaucomatous damage

Elevation of IOP in POAG is caused by increased resistance to aqueous outflow in the trabecular meshwork. Retinal ganglion cell death occurs predominantly through apoptosis (programmed cell death) rather than necrosis. The preterminal event is Ca^{++} influx into the cell body and an increase in intracellular nitric oxide. Glutamine metabolism has a profound effect on this process. The factors that influence the rate of cell death are multiple, but current opinion is polarized between ischaemic and mechanical aetiologies of damage.

1. **The ischaemic theory** postulates that compromise of the microvasculature with resultant ischaemia in the optic nerve head is responsible.
2. **The direct mechanical theory** suggests that raised IOP directly damages the retinal nerve fibres as they pass through the lamina cribrosa. It is likely that the pressure gradient around the optic nerve head rather than the absolute IOP is relevant in this context.

Screening

Population screening with tonometry alone is unsatisfactory, since it will label as 'normal' a significant number of cases with other features of POAG such as cupping and visual field loss. Even with the additional criterion of a vertical cup–disc ratio of >0.4, only 60% of potential POAG patients will be

identified. Until more accurate methods of mass screening are available, screening should therefore include visual field examination, tonometry and ophthalmoscopy. Individuals with a family history of glaucoma in first-degree relatives should be screened from the age of 40 years. Provided initial assessment is normal, subsequent review should be at 2-yearly intervals until the age of 50 years and then annually thereafter.

Clinical features

Symptoms

POAG is asymptomatic until significant loss of visual field has occurred. This is because damage occurs gradually and fixation is involved late in the course of the disease. Although the disease is almost invariably bilateral, progression is often asymmetrical. Patients therefore frequently present with significant visual field loss in one eye and less advanced disease in the other. Even highly self-analytical individuals may be unaware of large areas of visual field loss although occasionally early defects may be discovered by chance.

Signs

1. **Raised IOP.** This objective measurement has proved both a stumbling block and a great benefit in the diagnosis of POAG. Approximately 2% of the general population over the age of 40 years have IOPs > 24 mmHg and 7% have IOPs > 21 mmHg. However, only about 1% of these have glaucomatous visual field loss. This issue is further complicated by patients with 'normal' IOP (<22 mmHg) who develop glaucomatous visual field loss and cupping.
2. **Diurnal fluctuations in IOP** of up to 5 mmHg occur in approximately 30% of normals. In POAG this fluctuation is exaggerated and occurs in about 90% of cases. For this reason, a single pressure reading of 21 mmHg or less does not necessarily exclude the diagnosis of POAG, nor should a single reading of >21 mmHg do more than arouse suspicion. In order to detect fluctuations of IOP, it may be necessary to measure the IOP at different times during the day (phasing). Asymmetry of the IOP between the two eyes of 5 mmHg or more should arouse suspicion, since irrespective of the absolute value the eye with the higher reading may be abnormal.
3. **Optic disc changes.** POAG is often diagnosed after finding suspicious optic or asymmetrical discs on routine examination.
4. **Visual fields** show typical changes as previously described.
5. **Gonioscopy** shows a normal open angle.

Management

The primary aim of treatment is to prevent functional impairment of vision within the patient's lifetime by slowing the rate of ganglion cell loss closer to that of the normal population (approximately 5000/year). Currently the best method of achieving this goal is the lowering of IOP. Other modalities aimed at inhibition of ganglion cell apoptosis are currently under evaluation.

Baseline evaluation

Clear and concise records of baseline parameters are essential to monitor future progress.

1. **Visual acuity** and **refractive state.**
2. **Slit-lamp biomicroscopy**, paying attention to signs of secondary glaucomas which may masquerade as POAG.
3. **Applanation tonometry**, noting the time of day.
4. **Gonioscopy** should automatically follow applanation tonometry. However, if a coupling substance is required, gonioscopy should be delayed until the optic discs and visual fields have been assessed.
5. **Ophthalmoscopy** should be performed and the appearance of the disc documented by drawing and if possible also by photography.
6. **Perimetry.** The type of perimetry depends on the instrumentation available, the patient's age and visual acuity. In patients with significant lens opacities, perimetry should be performed with dilated pupils.

Patient instruction

A simple explanation should be offered concerning the nature of the disease and an explanatory booklet provided. The patient should be taught how to instil drops and the intervals between medications should be specified. At follow-up visits the patient's proficiency at instilling drops should be checked. In order to minimize systemic absorption the patient should be instructed either to perform lacrimal sac occlusion (by applying pressure at the medial canthus) or to close the eyes for about 3 minutes after instillation. Potential adverse effects should be explained and subsequently asked for at follow-up visits.

Grading of glaucomatous damage

1. **Mild damage** is characterized by early visual field defect (MD < −6 dB) (*see* Fig. 9.42) and mild cupping (Fig. 9.52).
2. **Moderate damage** is characterized by a definite arcuate scotoma (MD < −12 dB) (*see* Fig. 9.44) and moderate thinning of neuroretinal rim (Fig. 9.53).
3. **Severe damage** is characterized by extensive visual field loss (MD > −12 dB) (*see* Fig. 9.47) and marked cupping (Fig. 9.54).
4. **End-stage disease** is characterized by a small residual field and minimal residual neuroretinal rim (Fig. 9.55).

Treatment goals

1. **Target pressure.** It is assumed that the pre-treatment level of IOP has damaged the optic nerve and will continue to do so. An IOP level is identified below which further damage is considered unlikely (target pressure). The tar-

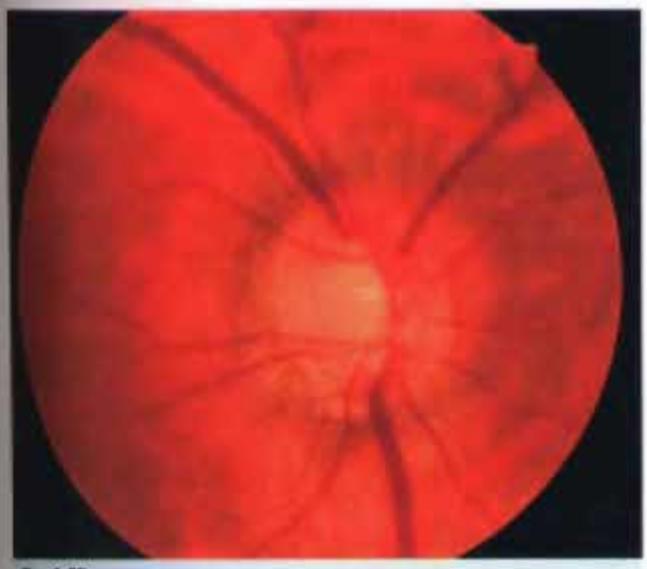

Fig. 9.52
Mild glaucomatous cupping

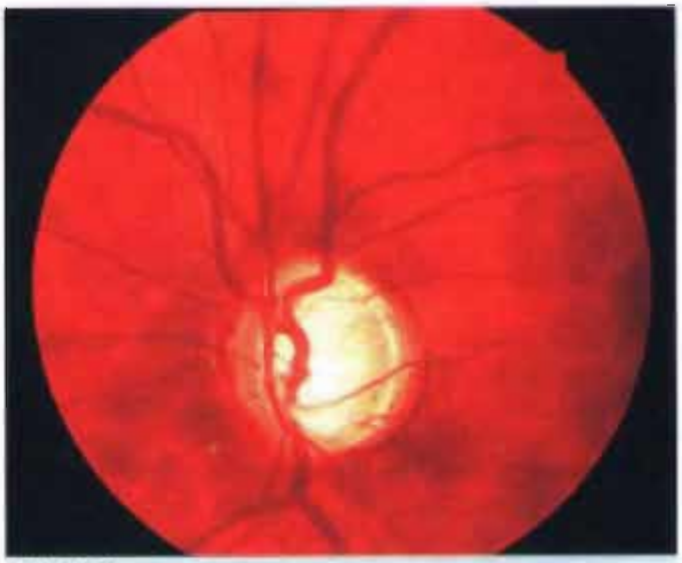

Fig. 9.54
Advanced glaucomatous cupping

Fig. 9.53
Moderate glaucomatous cupping

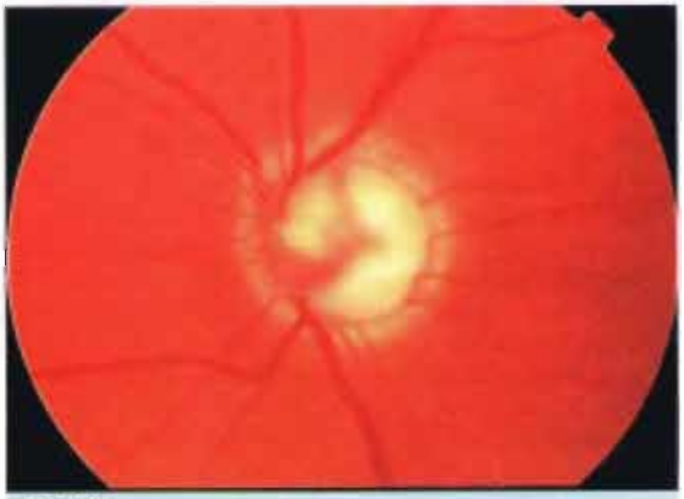

Fig. 9.55
Total glaucomatous cupping

pressure is identified taking into account the severity of existing damage, the level of IOP, the rapidity with which damage occurred (if that is known), as well as the age and general health of the patient. Therapy should maintain the IOP at or below the target level.

3. **Monitoring** is performed of the optic nerve and visual fields. In the event of further damage the target IOP is reset at a lower level. Although there is no 'safe' level, progression is uncommon if the IOP is <16 mmHg. As the disease progresses the degree of redundancy or 'reserve capacity' within the visual system diminishes and the loss of each remaining ganglion cell inflicts a greater impact on visual function. Lower target pressures are therefore required in patients with advanced disease.

Medical therapy

1. **Basic principles**
   - Any chosen drug should be used in its lowest concentration and as infrequently as possible consistent with the desired therapeutic effect.
   - Ideally the drug with the fewest potential side effects should be used.
   - Initial treatment is usually with one drug.
2. **Follow-up** should be after 4 weeks.
   - A fall in IOP of >4 mmHg is considered significant (i.e. caused by the drug as opposed to chance fluctuation) but may not always be sufficient (depending on treatment goals).
   - If the response is satisfactory subsequent assessment is after 1 month and at 3 or 4-monthly intervals thereafter.
   - If the response is unsatisfactory the initial drug is withdrawn and another substituted.

- If the response is still unsatisfactory yet another drug is added or a combined preparation (i.e. timolol–latanoprost or timolol–dorzolamide) substituted. When two separate drugs are used the patient should be instructed to wait 5 minutes before instilling the second drug to prevent washout of the first drug.

3. **Perimetry.** If control is good and the appearance of the optic disc stable, annual perimetry is sufficient.
4. **Gonioscopy** should also be performed annually because the anterior chamber gradually shallows with age.
5. **Causes of failure**
   - Inappropriate target pressure. If the IOP runs in the upper part of the statistically normal range, progressive field loss is common.
   - Non-compliance with therapy occurs in at least 25% of patients.
   - Wide fluctuations in IOP frequently occur in patients treated medically.

Laser trabeculoplasty

In this procedure discrete argon or diode laser burns are applied to the trabeculum to enhance aqueous outflow and lower IOP. The therapeutic effect is often transient, lasting a few years, so that laser therapy may merely defer the need for filtration surgery. The following are the main indications:

1. **Avoidance of polypharmacy**, usually with more than two preparations. In this situation laser therapy may be considered as a substitute for another drug.
2. **Avoidance of surgery**
   - In elderly patients in whom laser therapy may defer the need for surgery to beyond life expectancy.
   - In black patients in whom filtration surgery carries a poorer prognosis.
3. **As primary therapy** in patients who are expected not to comply with medical therapy. Since IOP reduction with laser is seldom greater than 30%, an IOP > 28 mmHg is unlikely to be adequately controlled by laser alone.
4. **Patients non-compliant with medical therapy.**

Trabeculectomy

This involves the surgical creation of a fistula between the angle of the anterior chamber and the sub-Tenon space, which allows egress of aqueous from the anterior chamber into a 'drainage bleb' under the upper eyelid. Progressive damage is less likely after trabeculectomy than with medical therapy because the resultant IOP is often significantly lower and less likely to fluctuate. The timing of surgery depends on the amount of visual loss that has occurred, the rapidity of deterioration and life expectancy. The following are the main indications:

1. **Failed medical therapy** and/or **laser trabeculoplasty.**
2. **Unsuitability** for laser therapy due to poor patient cooperation or inadequate visualization of the trabeculum (narrow angle, corneal opacification).
3. **Advanced disease** requiring a very low target pressure may benefit from early surgery.

NB: Some ophthalmologists in the UK would consider trabeculectomy when a single topical medication fails to achieve the target pressure or prevent progressive optic nerve damage.

Normal-tension glaucoma

Definition

Normal-tension glaucoma (NTG), also referred to as low-tension glaucoma, is a variant of POAG. Predominantly a disease of the elderly, it is more common in females. It is characterized by:

- A mean IOP equal to or less than 21 mmHg on diurnal testing.
- Glaucomatous optic disc damage and visual field loss.
- Open drainage angle on gonioscopy.
- Absence of secondary causes for glaucomatous optic disc damage.

NB: The classification of POAG into two types (i.e. normal-tension and high-tension) is based on an epidemiologically derived normal IOP. It is therefore essentially an arbitrary division and may not have significant clinical value. The prevalence of NTG in individuals over the age of 40 years is 0.2% and the condition accounts for 16% of all cases of POAG.

Signs

1. **The IOP** is usually in the high teens, but may rarely be in the low teens. In asymmetrical disease the more damaged disc corresponds to the eye with the higher IOP.
2. **Optic nerve head**
   - Both glaucomatous cupping or parapapillary changes are identical to those seen in POAG.

Fig. 9.56
Moderate glaucomatous cupping with a splinter haemorrhage.

- Splinter haemorrhages at the disc margin (Fig. 9.56) are more frequent in NTG and may indicate progressive damage of the retinal nerve fibre layer.
- Acquired optic disc pits characterized by localized excavations of the lamina cribrosa are also more frequent.

3. **Visual field defects** are essentially the same as in POAG although it has been suggested that in NTG they tend to be closer to fixation, deeper, steeper and more localized. In some patients, even without treatment, field changes are non-progressive. However, because of frequent delay in diagnosis, patients with NTG tend to present with more advanced damage than those with POAG. Patients with unilateral field defects have a 40% chance of developing field loss in the fellow eye within 5 years.
4. **Other characteristics** which are more common in NTG than in POAG include:
   - Peripheral vascular spasm on cooling (Raynaud phenomenon).
   - Migraine may be more common, although this has not been confirmed in a population-based survey.
   - Nocturnal systemic hypotension and overtreated systemic hypertension.
   - Reduced blood flow velocity in the ophthalmic artery when measured with transcranial Doppler ultrasonography.
   - Paraproteinaemia and the presence of serum autoantibodies.

Treatment

This is indicated only in patients with documented progressive visual field loss. The aim is to reduce the IOP by at least 30%.

1. **Medical** treatment. Betaxolol may be the drug of choice because of its beneficial effects on optic nerve blood flow in addition to its IOP-lowering properties. However, prostaglandin analogues tend to have a greater ocular hypotensive effect in eyes with normal IOP.
2. **Trabeculectomy** should be considered, in at least one eye, if progressive field loss occurs despite IOP in the lower teens.
3. **Systemic calcium channel blockers** (e.g. nifedipine) may be considered in younger patients and in those with early disease. Ideally, peripheral vasospasm should be confirmed by nailfold capilloscopy before commencing treatment. Long-term therapy is warranted only if visual fields remain stable after a short-term (2–3 months) therapeutic trial.
4. **Monitoring of systemic blood pressure** for 24 hours. If a significant nocturnal drop is detected, it may be necessary to avoid anti-hypertensive medication, especially if taken prior to bedtime.

Differential diagnosis

1. **POAG** presenting with normal IOP because of a wide diurnal fluctuation. This can be excluded by phasing (diurnal IOP curve) over an 8-hour period in order to detect a pressure spike of >21 mmHg.
2. **Congenital optic disc anomalies** such as large optic disc pits or colobomas may be mistaken for acquired glaucomatous cupping.

Primary angle-closure glaucoma

Introduction

Primary angle-closure glaucoma (PACG) is a condition in which elevation of IOP occurs as a result of obstruction of aqueous outflow by partial or complete closure of the angle by the peripheral iris. Unlike POAG, the diagnosis depends largely on examination of the anterior segment and careful gonioscopy. A normal optic nerve head and visual field do not preclude a diagnosis of PACG. This disease occurs in anatomically predisposed eyes and is frequently bilateral, although presentation of the acute form is often unilateral. Based on the mechanism of angle closure, two forms of PACG are recognized: (a) *pupillary block* and (b) *plateau iris syndrome*, which is rare.

Risk factors

1. **Age**. The average age at presentation is about 60 years; prevalence increases thereafter.
2. **Gender**. Females are more commonly affected than males by a ratio of 4:1.
3. **Race**. In caucasians the condition accounts for about 6% of all glaucomas and it affects approximately 1:1000 individuals over the age of 40 years. PACG is more common in South-East Asians, Chinese and Eskimos and is uncommon in black people.
4. **Family history**. First-degree relatives are at increased risk because predisposing anatomical factors are often inherited (*see* below).

Anatomical predisposing factors

1. **Relatively anterior location of the iris–lens diaphragm.**
2. **Shallow anterior chamber.**
3. **Narrow entrance to the chamber angle.**
   Proximity of the peripheral iris to the cornea facilitates angle closure. The following three interrelated factors are responsible for these characteristics:
   a. *Lens size*. The lens is the only ocular structure which continues to increase in size throughout life. Axial (anteroposterior) growth brings its anterior surface closer to the cornea, while equatorial growth slackens the suspensory ligament, allowing the iris–lens diaphragm to move anteriorly. Both these factors cause gradual and progressive shallowing of the anterior chamber. Eyes with PACG have shallower anterior chambers than normal eyes, and women have shallower anterior chambers than men.

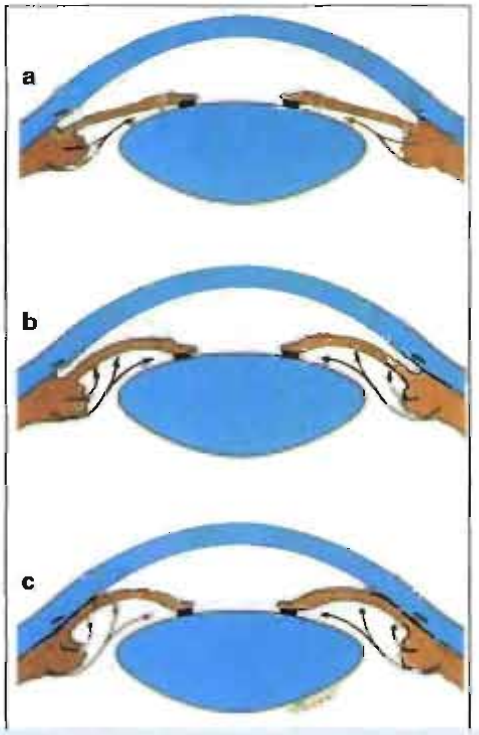

Fig. 9.57
Mechanism of angle closure. (a) Relative pupil block; (b) iris bombé; (c) iridocorneal contact

b. Corneal diameter. Anterior chamber depth and angle width are related to the corneal diameter. Eyes with PACG have corneal diameters 0.25 mm smaller than normal.

c. Axial length. The position of the lens and the corneal diameter are related to the axial length of the globe. A short eye, which is also frequently hypermetropic, has a small corneal diameter and a relatively anteriorly located lens. For this reason eyes with nanophthalmos are at increased risk of angle-closure glaucoma.

Pathogenesis

The pathogenesis of acute PACG is incompletely understood. Normally the pressure in the posterior chamber exceeds that in the anterior chamber due to a physiological degree of resistance at the pupil, since the iris rests posteriorly on the anterior lens capsule.

1. **The dilator muscle theory** postulates that contraction of the dilator pupillae exerts a posterior vector. This increases the amount of apposition between the iris and the anteriorly located lens, enhancing the degree of physiological pupil block (Fig. 9.57a). Simultaneous dilatation of the pupil renders the peripheral iris more flaccid. The pupil block causes the pressure in the posterior chamber to increase and the peripheral iris bows anteriorly (iris bombé) (Fig. 9.57b). Eventually the iris touches the posterior corneal surface, obstructing the angle and the IOP rises (Fig. 9.57c).
2. **The sphincter muscle** theory postulates that the sphincter pupillae is the prime culprit in precipitating angle closure. The pupillary blocking force of the sphincter is greatest when the diameter of the pupil is approximately 4 mm.

Classification

Although PACG can be divided into five overlapping stages the condition does not necessarily progress from one stage to the next in an orderly sequence. In practice, a combination of these clinical stages is often seen:

1. **Latent.**
2. **Subacute (intermittent).**
3. **Acute congestive.**
4. **Postcongestive.**
5. **Chronic.**
6. **Absolute** is the end-stage of acute congestive PACG in which the eye is completely blind and will not be discussed further.

Latent angle-closure glaucoma

Clinical features

This is a retrospective diagnosis, only made with any degree of certainty in one eye during an attack of acute congestive glaucoma in the other. It can therefore often only be *suspected* prospectively. Essentially, the term 'latent angle closure' implies an anatomically predisposed eye.

1. **Symptoms** are absent.
2. **Slit-lamp biomicroscopy**
   - Axial anterior chamber depth is less than normal.

NB: This can also be demonstrated by shining a penlight across the eye from the temporal side. Due to the convexity of the iris–lens diaphragm, the nasal iris manifests a crescentic shadow, appearing dark relative to the temporal iris (the eclipse sign) (Fig. 9.58).

Fig. 9.58
'Eclipse' sign elicited by directing a light across the anterior chamber from the temporal side and noting a shadow on the nasal side (Courtesy of J. Salmon)

Fig. 9.59
Convex-shaped iris–lens diaphragm

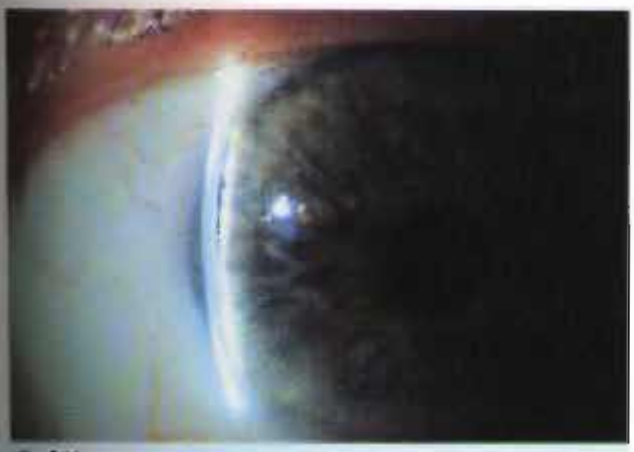

Fig. 9.60
Close proximity of iris to the peripheral cornea

- Convex-shaped iris–lens diaphragm (Fig. 9.59).
- Close proximity of the iris to the cornea (Fig. 9.60).

3. **Gonioscopy** shows an 'occludable' angle in which the pigmented trabecular meshwork is not visible (Shaffer grade 1 or 0) without indentation or manipulation in at least three quadrants.
4. **The clinical course** without treatment may be as follows:
   - The IOP may remain normal.
   - Acute or subacute angle closure may develop.
   - Chronic angle closure may develop, without passing through subacute or acute stages.

Treatment

- If one eye has had acute or subacute PACG, the fellow eye should undergo prophylactic peripheral laser iridotomy because, without treatment, the risk of an acute pressure rise during the next 5 years is about 50%.
- If both eyes have latent PACG, no parameter or provocative test is sufficiently sensitive or accurate to determine whether acute PACG will later develop. However, since the risks of laser iridotomy are small, if carefully undertaken laser treatment may be considered.

NB: Although prophylactic laser iridotomy will prevent an acute attack, 15% of eyes may develop a late rise in IOP.

Subacute angle-closure glaucoma

Subacute (intermittent) PACG occurs in a predisposed eye with an occludable angle in association with intermittent pupillary block. Rapid closure of the angle results in sudden increase in IOP. The pupillary block is then spontaneously relieved, the angle opens and the IOP returns to normal. Attacks may be precipitated by physiological mydriasis (watching television in a dark room), or by physiological shallowing of the anterior chamber when the patient assumes a prone or semiprone position (when sewing or reading). Emotional stress may occasionally be a precipitating factor.

1. **Diagnosis** is based on a characteristic history of transient blurring of vision associated with haloes around lights due to corneal epithelial oedema (the blue end of the spectrum being nearer the source). There may also be associated ocular discomfort or frontal headache. The attacks are recurrent and are usually broken after 1–2 hours by physiological miosis (exposure to bright sunlight or sleep). During an attack the eye is usually white and in between attacks looks normal although the angle is narrow.
2. **The clinical course** without treatment is variable. Some eyes develop an acute attack and others may develop chronic angle closure.
3. **Treatment** is with prophylactic peripheral laser iridotomy.

Acute congestive angle-closure glaucoma

This is a sight-threatening emergency, involving painful loss of vision, due to sudden and total closure of the angle.

Clinical features

1. **Symptoms** in classical cases include rapidly progressive unilateral visual loss associated with periocular pain and congestion. Nausea and vomiting may occur in severe cases.

NB: It is important to note the variability of symptoms in an attack of acute angle-closure. Some patients, particularly black people, in whom the condition is uncommon, have remarkably little pain and no congestion despite very high IOPs, the only symptom being impairment of vision. Moreover, a history of transient blurring and haloes characteristic of previous intermittent attacks is often absent.

2. **Slit-lamp biomicroscopy**
   - 'Ciliary' flush due to injection of the limbal and conjunctival blood vessels.

Fig. 9.61
Corneal oedema in acute angle-closure glaucoma

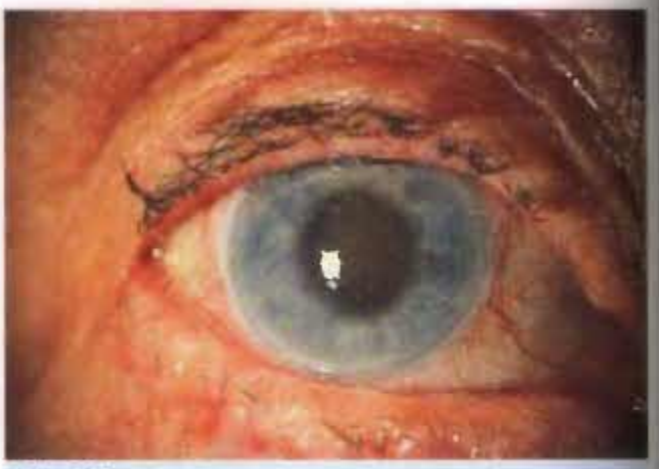

Fig. 9.63
Dilated and oval pupil in acute angle-closure glaucoma

Fig. 9.62
Corneal oedema and a shallow anterior chamber in acute angle-closure glaucoma

Fig. 9.64
Gonioscopy showing complete angle closure

- Corneal oedema with epithelial vesicles and stromal thickening (Fig. 9.61).
- Shallow anterior chamber with peripheral iridocorneal contact (Fig. 9.62).
- Aqueous flare and cells may be seen once the corneal oedema has resolved.
- The pupil is vertically oval, fixed in the semi-dilated position (Fig. 9.63) and unreactive to both light and accommodation.
- The iris blood vessels are dilated.
- The IOP is severely elevated (50–100 mmHg).

3. **Gonioscopy** may need to be deferred until the corneal oedema has resolved, either with ocular hypotensive medication or with topical glycerine or hypertonic saline ointment. It is, however, vital to perform this examination in the fellow eye, which usually exhibits characteristics of latent angle closure. The affected eye shows complete peripheral iridocorneal contact (Shaffer grade 0) (Fig. 9.64).

NB: The diagnosis should be questioned if the fellow eye does not show a narrow angle on gonioscopy.

4. **Ophthalmoscopy**, when possible, shows optic disc oedema and hyperaemia.

Differential diagnosis

1. **Secondary acute angle closure** due to an intumescent (swollen) or dislocated lens.
2. **Neovascular glaucoma** may occasionally cause a sudden onset of pain and congestion.
3. **Glaucomatocyclitic crisis** may cause severe elevation of IOP with pain and haloes.
4. **Other causes of headache** around the eye such as migraine or migrainous neuralgia (cluster headache).

Immediate treatment

1. **Acetazolamide** 500 mg intravenously and 500 mg orally (not slow-release) provided there is no vomiting.

NB: Check for sulphonamide allergy.

2. **Topical therapy**
   - Pilocarpine 2% two drops to both eyes.

- Dexamethasone (or equivalent) q.i.d.
- A beta-blocker if there is no systemic contraindication.

3. **Analgesia** and anti-emetics as required.
4. **Patient to lie supine** for 1 hour.

> **NB:** Laser iridotomy may also be effective in relatively mild cases.

After 1 hour

Pilocarpine 2% should be repeated half to 1 hour after commencement of treatment, by which time reduction of iris ischemia and lowering of IOP allows the sphincter pupillae to respond to the drug. There is no place for 'intensive' miotic therapy. The fellow eye is also treated prophylactically with pilocarpine 1% q.i.d. until a laser iridotomy can be performed.

After further 30 minutes

If the IOP has not fallen to below 35 mmHg, oral 50% glycerol may be administered (1 g/kg) (with caution in diabetics) and fluid intake limited for maximum effect. If the patient is unable to tolerate oral glycerol, 20% mannitol (1–2 g/kg) may be given intravenously over 45 minutes.

> **NB:** A high IOP unresponsive to ocular hypotensive medication may sometimes respond to axial corneal indentation with a squint hook or a Zeiss goniolens. If angle closure is appositional, this allows aqueous humour to force its way between the iris and cornea to the angle, thus opening it and giving access to the trabecular meshwork. This measure may occasionally break a cycle of elevating IOP and allow it to fall.

Nd:YAG laser iridotomy

1. **The purpose** of peripheral laser iridotomy is to re-establish communication between the posterior and anterior chambers by making an opening in the peripheral iris. This will be successful only if less than 180° of the angle is closed by permanent peripheral anterior synechiae.
2. **Timing** varies with the severity of the attack and the rapidity of corneal clearing. Iridotomy has been advocated as initial treatment to break pupil block but may be difficult until the corneal thickening and iris congestion have settled (usually 48 hours). After an explanation has been given, it may be appropriate to perform a prophylactic laser iridotomy on the fellow eye in the interim period. Laser iridotomy is effective in about 75% of eyes with acute angle-closure glaucoma. Unresponsive cases may require trabeculectomy.

> **NB:** It is important to confirm that the angle is open after peripheral iridotomy even if the IOP is normal.

Postcongestive angle-closure glaucoma

Clinical settings

Postcongestive angle-closure glaucoma refers to the aftermath of an attack of acute angle closure. It may be seen in the following three clinical settings:

1. **Postsurgical.** Here the IOP is normalized by successful peripheral iridotomy. Occasionally, even after peripheral iridotomy, with the angle open 180° or more, IOP may still be elevated due to associated trabecular damage. Medical therapy or trabeculectomy may be needed to control the IOP.
2. **Spontaneous angle reopening** without treatment may occur in a few cases; management is as for intermittent angle closure.
3. **Ciliary body shutdown.** This involves temporary cessation of aqueous secretion due to ischaemic damage to the ciliary epithelium. Subsequent recovery of ciliary function may lead to chronic elevation of IOP with cupping and field loss.

Clinical features

1. **Slit-lamp biomicroscopy**
   - Folds in Descemet membrane (Fig. 9.65), if the IOP has been reduced rapidly.
   - Fine pigment granules on the corneal endothelium.
   - Aqueous flare and cells.
   - Stromal iris atrophy with a spiral-like configuration; fine pigment granules on the surface of the iris (Fig. 9.66).
   - A fixed and semi-dilated pupil due to a combination of paralysis of the sphincter and posterior synechiae (Fig. 9.67).
   - Glaukomflecken characterized by small, grey-white, anterior subcapsular or capsular lens opacities in the pupillary zone are diagnostic of a previous congestive attack (Fig. 9.68). These represent focal necrosis of the lens epithelium.
   - The IOP may be normal, subnormal or elevated.

Fig. 9.65
Folds in Descemet membrane and residual corneal oedema in postcongestive angle-closure glaucoma

Fig. 9.66
Stromal iris atrophy in postcongestive angle-closure glaucoma

Fig. 9.67
Posterior synechiae in postcongestive angle-closure glaucoma

Fig. 9.68
Anterior subcapsular lens opacities (glaukomflecken) in postcongestive angle-closure glaucoma

2. **Gonioscopy** shows a narrow angle which may be open or partly closed. If open, trabecular hyperpigmentation may be present. A straight line of pigment may be seen anterior to Schwalbe line at the site of previous iridocorneal contact.

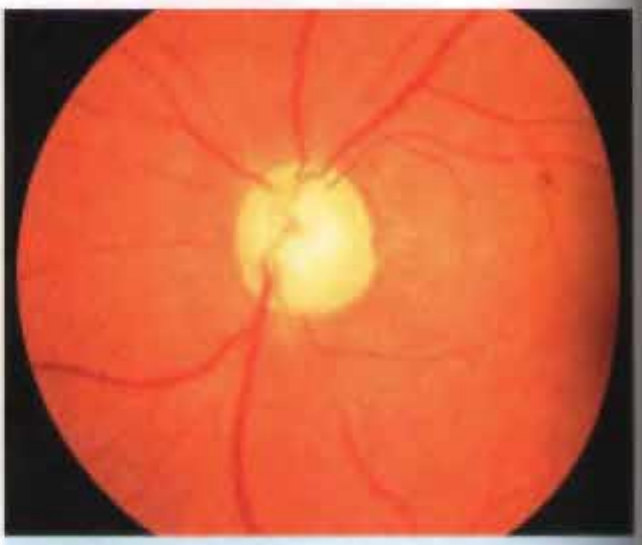

Fig. 9.69
Optic atrophy following acute angle-closure glaucoma (Courtesy of J. Salmon)

Fig. 9.70
'Creeping' angle closure (Courtesy of J. Salmon)

3. **Ophthalmoscopy** may reveal congestion of the optic disc and choroidal folds if the IOP is very low. The disc may be atrophic as a result of infarction (Fig. 9.69).

Chronic angle-closure glaucoma

Pathogenesis

1. **Type 1** (creeping) is caused by gradual and progressive synechial angle closure which always starts superiorly and spreads circumferentially (Fig. 9.70). This may be caused by anteriorly situated ciliary processes; many eyes have a plateau iris configuration (*see* below).
2. **Type 2** is caused by synechial angle closure as a result of intermittent (subacute) attacks secondary to pupillary block.
3. **Type 3** (mixed) is caused by a combination of POAG with narrow angles usually associated with the long-term use of miotics. It is commonly diagnosed on gonioscopy at the time of laser trabeculoplasty.

Clinical features

These are similar to POAG. Gonioscopy shows a variable degree of angle closure, although permanent peripheral anterior synechiae do not usually develop until late. The diagnosis will be missed unless gonioscopy is performed on all glaucomatous eyes.

Treatment

1. **Type1** (creeping) is initially treated by laser iridotomy to eradicate any element of pupil block. Any residual elevation of IOP is then treated medically. If this fails, trabeculectomy will be required.
2. **Type 2** will already have undergone iridotomy. Medical therapy should be added as necessary.
3. **Type 3** (mixed) will already be on medical therapy for POAG and should be treated by laser iridotomy.

Plateau iris

1. **Plateau iris configuration** is characterized by a closed anterior chamber angle in association with a flat iris plane and a deep central anterior chamber. An anterior position of the ciliary processes results in an abnormal configuration of the peripheral iris. Although this mechanism of angle closure is rare in white people, it is not uncommon in South-East Asians.
2. **Plateau iris syndrome** describes acute angle closure which occurs with pupillary dilatation despite a patent iridotomy. The syndrome tends to occur at a younger age than angle closure with pupillary block. When the pupil dilates, the peripheral iris becomes 'bunched up' and occludes the trabeculum (Fig. 9.71). All the features of acute congestive angle closure are present except that the axial anterior chamber depth is normal and the iris plane is flat rather than convex.
3. **Treatment** is with pilocarpine 1% drops after the performance of a laser peripheral iridotomy. It may also be possible to flatten the 'hump' in the peripheral iris with argon laser (gonioplasty).

Fig. 9.71
Angle closure in the plateau iris syndrome

Pseudoexfoliative glaucoma

Pseudoexfoliation syndrome

Introduction

The pseudoexfoliation (PEX) syndrome is a relatively common but easily overlooked cause of chronic open-angle glaucoma. When an eye with PEX develops a secondary trabecular block glaucoma the condition is referred to as PEX glaucoma or glaucoma capsulare. Although PEX is more common in females, males appear to be at higher risk of developing glaucoma. Although no clear hereditary pattern has been established, the condition is a particularly common cause of glaucoma in Scandinavia and is also associated with a gene locus at 2p16. PEX should be differentiated from very rare true exfoliation, which involves lamellar splitting of the lens capsule secondary to infra-red damage.

Pathogenesis

In PEX a grey-white, fibrillogranular, extracellular, matrix material similar to amyloid, is deposited on the anterior lens capsule, zonules, ciliary body, iris, trabeculum, anterior vitreous face and conjunctiva. Secondary trabecular block glaucoma is thought to result from a combination of 'clogging up' of the trabeculum by pseudoexfoliative material and/or pigment released from the iris, as well as trabecular endothelial dysfunction. The material is produced by abnormal basement membranes of ageing epithelial cells in the trabeculum, equatorial lens capsule, iris and ciliary body.

> ***NB:*** In addition to its occurrence within the eye, exfoliative fibrillopathy has been reported in skin and visceral organs, suggesting that the PEX syndrome may be an ocular manifestation of a systemic disorder.

Clinical features

1. **Cornea**
   - *a.* *PEX* on the endothelium may mimic inflammatory keratic precipitates.
   - *b.* ***Pigment deposition*** on the endothelium is usually diffuse although occasionally it may take the form of a Krukenberg spindle (*see* below).
   - *c.* ***Endothelial cells*** are reduced in number and morphologically abnormal with a propensity to decompensation, even with a moderate rise in IOP.
2. **Anterior chamber** may exhibit mild aqueous flare due to breakdown of the iris blood–aqueous barrier (pseudouveitis).
3. **Iris**
   - *a.* *PEX* on the pupillary margin (Fig. 9.72).
   - *b.* ***Sphincter atrophy*** characterized by 'moth-eaten' transillumination defects (Fig. 9.73), most evident in

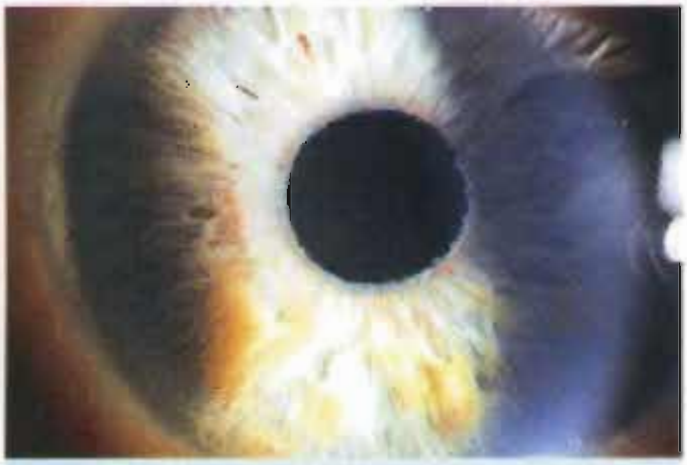

Fig. 9.72
Pseudoexfoliative material on the pupillary border

Fig. 9.75
Central disc and a peripheral band of pseudoexfoliative material

Fig. 9.73
Sphincter atrophy seen on transillumination in the pseudoexfoliation syndrome

Fig. 9.76
Peripheral band of pseudoexfoliative material

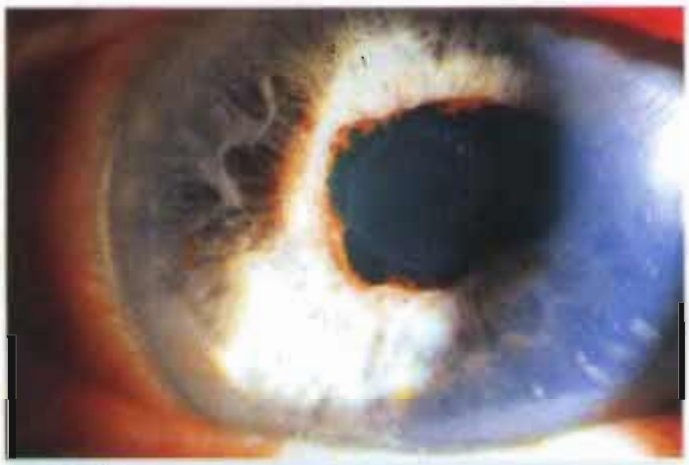

Fig. 9.74
Posterior synechiae in the pseudoexfoliation syndrome

eyes with pupillary ruff defects. It is associated with poor pupillary dilatation.

*c. **Pigment dispersion*** may be precipitated by mydriasis or surgery. On the iris sphincter the pigment granules have a whorl-like configuration whereas in the periphery they are scattered more diffusely.

*d. **Intrastromal haemorrhages*** may develop on pharmacological mydriasis.

*e. **Posterior synechiae*** may contribute to poor pupillary dilatation (Fig. 9.74).

4. Lens

*a. **PEX*** on the anterior lens surface. The constant rubbing of the pupil scrapes the material off the mid-zone of the lens, giving rise to a central disc and a peripheral band of PEX, with a clear zone in between (Fig. 9.75). The central disc is translucent, well demarcated and its edges may contain rolled-up fragments. The margin of the central disc may be ill defined and difficult to distinguish, and in some cases the disc is absent. The peripheral band is granular and has a well-delineated inner border with multiple radial striations (Fig. 9.76). It can be detected only under mydriasis.

*b. **Zonular instability*** is caused by alterations in the zonules and their insertions into the ciliary body and lens. This may give rise to phacodonesis, lens subluxation, dislocation and an increased incidence of zonular dialysis and vitreous loss during cataract surgery.

*c. **Nuclear cataract*** occurs commonly.

Fig. 9.77
Trabecular hyperpigmentation with a Sampaolesi line in the pseudoexfoliation syndrome

3. Gonioscopy
   a. *Trabecular hyperpigmentation* is common and is usually most marked inferiorly. The pigment lies on the surface of the trabeculum and has a patchy distribution (Fig. 9.77). A scalloped band of pigment running on to or anterior to Schwalbe line (Sampaolesi line) is also frequently seen.
   b. *PEX* may be deposited in the trabeculum and give rise to a 'dandruff-like' appearance.
   c. *Narrow angles* are present in some cases; even in eyes with wide open angles, the IOP may become elevated when the pupil is dilated.

Pseudoexfoliative glaucoma

Risk factors

- The cumulative risk of glaucoma in eyes with pseudoexfoliation is 5% at 5 years and 15% at 10 years. Individuals with PEX should be informed of this risk and advised to undergo annual ocular examination.
- A patient with unilateral pseudoexfoliative glaucoma and PEX in the fellow eye is at high risk (50% in 5 years) of developing glaucoma in the fellow eye.
- A patient with unilateral pseudoexfoliation glaucoma who does not have PEX in the fellow eye is at very small risk of developing glaucoma in the normal eye.

Clinical features

1. **Presentation** is usually in the seventh decade, which is later than POAG.
2. **Signs.** The majority of patients have a chronic open-angle glaucoma which is usually unilateral. Occasionally the IOP may rise acutely despite the angle being wide open; this may be confused with primary angle-closure glaucoma. The degree of angle hyperpigmentation correlates with the severity of glaucoma.

Treatment

1. **Medical** treatment is the same as for POAG. However, despite initial success in most cases, there is a high incidence of late failure and patients are likely to require laser therapy or surgery.
2. **Laser trabeculoplasty** is particularly effective, possibly because of trabecular hyperpigmentation. However, after an initial good response a gradual late rise of IOP occurs so that after 4 years the results are the same as in POAG.
3. **Early trabeculectomy** may be advantageous. It has the same success rate as in POAG, with no unusual complications.

Prognosis

This is poorer than with POAG, since the IOP is often significantly elevated and may also exhibit great fluctuation so that severe damage may develop rapidly. It is therefore important to monitor patients closely until the IOP is brought under control.

Pigmentary glaucoma

Pigment dispersion syndrome

The pigment dispersion syndrome (PDS) is a usually bilateral condition characterized by the liberation of pigment granules from the iris pigment epithelium and their deposition throughout the anterior segment. PDS primarily affects white people, and may be inherited as an autosomal dominant trait with variable penetrance. Two gene loci have been identified on chromosomes 7 and 8. Myopia predisposes to the phenotypical manifestations and the development of a secondary open-angle 'pigmentary' glaucoma.

Pathogenesis

Pigment shedding is caused by the mechanical rubbing of the posterior pigment layer of the iris against packets of lens zonules as a result of excessive posterior bowing of the mid-peripheral portion of the iris. The pigment epithelium itself may be abnormally susceptible to shedding; in some patients strenuous exercise may precipitate episodes of pigment dispersion associated with a rise in IOP. The pigment granules are released into the aqueous humour, dispersed by aqueous currents and deposited on all anterior chamber structures, including the zonular fibres and ciliary body. Elevation of IOP appears to be caused by pigmentary obstruction of the intertrabecular spaces and damage to the trabeculum secondary to denudation, collapse and sclerosis. It is postulated that an increase in anterior chamber pressure (relative to the posterior chamber) occurs due to 'reverse' pupil block, with resultant posterior bowing of the iris and irido-zonular touch. This is supported by

Fig. 9.78
Krukenberg spindle in the pigment dispersion syndrome

Fig. 9.81
Mid-peripheral iris transillumination defects in the pigment dispersion syndrome

Fig. 9.79
Very deep anterior chamber in the pigment dispersion syndrome

Fig. 9.82
Trabecular hyperpigmentation in the pigment dispersion syndrome

Fig. 9.80
Pigment granules on the iris in the pigment dispersion syndrome

the observation that neutralization of reverse pupil block with peripheral iridotomy flattens the iris and decreases irido-zonular contact.

Clinical features

1. **The cornea** manifests pigment deposition on the endothelium in a vertical spindle-shaped distribution (Krukenberg spindle) (Fig. 9.78). The size and density of the deposit are usually proportional to the extent of associated iris atrophy. The Krukenberg spindle, although common, is neither universal nor pathognomonic of PDS, and in long-standing cases may be more difficult to detect because it tends to become smaller and lighter in color.
2. **The anterior chamber** is very deep (Fig. 9.79); pigment granules may be seen floating in the aqueous.
3. **Iris**
   a. ***Fine pigment granules*** are preferentially deposited within its furrows (Fig. 9.80). This may render the iris progressively darker, giving rise to heterochromia, often in asymmetrical involvement.
   b. ***Iris pigment epithelial atrophy*** due to shedding of pigment from the mid-periphery gives rise to characteristic radial slit-like transillumination defects (Fig. 9.81). If asymmetrical, the eye with more atrophy may exhibit a slightly larger pupil.

4. **Lens.** The anterior surface may show pigment deposits. On the posterior surface the pigment tends to form a line at the site of vitreolenticular adhesion.
5. **Gonioscopy**
   a. Wide ***open angle*** with characteristic mid-peripheral iris concavity that may increase with accommodation.
   b. ***Trabecular hyperpigmentation*** is most marked over the posterior trabeculum (Fig. 9.82). In contrast with the coarse pigmentation seen in PEX, that in PDS is finer and appears to lie both on and within the trabecular meshwork. It also has a more homogeneous appearance and forms a dense band involving the entire circumference of the angle uniformly. Pigment may also be seen on or anterior to Schwalbe line.
6. **The fundus** may show areas of lattice degeneration which may be responsible for an increased risk of retinal detachment. Pigment deposition may also be seen in the peripheral retina.

Pigmentary glaucoma

Risk factors

Up to one-third of patients with PDS eventually develop ocular hypertension or chronic open-angle glaucoma. Men are affected twice as frequently as women. It is therefore important to regularly follow patients with the condition, particularly myopic males with Krukenberg spindles. However, initial IOP, cup–disc ratio and degree of trabecular hyperpigmentation are not helpful in identifying those who will eventually develop glaucoma. Patients with pigmentary glaucoma have an increased incidence of steroid responsiveness. Although PDS is rare in black patients, they are at increased risk of developing glaucoma which is of a more severe form than that found in white patients.

Clinical features

1. **Presentation** is usually with chronic glaucoma most commonly in the third and fourth decades, although in women it tends to develop 10 years later. Occasionally the sudden release of pigment granules following vigorous movement of the pupil or strenuous physical exercise may precipitate an acute rise in IOP, with corneal oedema and haloes.
2. **The IOP** may initially be very unstable, so that a single normal reading does not exclude glaucoma. Some patients exhibit higher levels and wider fluctuations of IOP than in POAG and at the time of diagnosis it is common to find advanced disease in one eye and relatively mild damage in the other.

Treatment

1. **Medical** treatment is similar to that of POAG. Miotics may theoretically be of particular benefit because they increase irido-zonular contact in addition to facilitating aqueous outflow. However, they carry the disadvantage of exacerbating myopia.
2. **Laser trabeculoplasty** is often initially effective, although younger patients appear to respond better. It is important not to over-treat eyes with heavily pigmented angles and to start at a relatively low-power laser setting. At least one-third of patients will require trabeculectomy within 5 years of laser trabeculoplasty.
3. **Laser iridotomy** may be effective in preventing further pigment deposition by reversing iris concavity.
4. **Trabeculectomy** is required in patients unresponsive to medical therapy and laser trabeculoplasty, although the results are less predictable in younger patients. Operative use of adjunctive antimetabolites may improve surgical outcome. A higher percentage of patients with pigmentary glaucoma require surgery as compared with POAG and men require it earlier.

Prognosis

This is relatively good and over time the control of IOP becomes easier. Occasionally the IOP may spontaneously revert to normal. This may or may not be associated with a decrease in trabecular pigmentation. Patients with such undetected previous pigmentary glaucoma may later be erroneously diagnosed as having normal-tension glaucoma.

Differential diagnosis

1. **POAG** may be associated with a hyperpigmented trabeculum. However, the pigment tends to be concentrated in the inferior sector of the angle, unlike in the PDS. Patients with POAG are also usually older and lack Krukenberg spindles and iris transillumination defects.
2. **Pseudoexfoliative glaucoma** may exhibit trabecular hyperpigmentation and pigment dispersion. However, transillumination defects are evident at the margin of the pupil rather than in the periphery. In contrast to pigmentary glaucoma, pseudoexfoliative glaucoma usually affects patients over the age of 60 years, is unilateral in 50% of cases and has no predilection for a myopic refractive error.
3. **Pseudophakic pigmentary glaucoma** occurs in the context of rubbing of the haptics and optics of a posterior chamber intraocular lens against the posterior surface of the iris, with resultant pigment dispersion and outflow obstruction.
4. **Anterior uveitis** may result in trabecular hyperpigmentation and iris atrophy. Clustered small old pigmented keratic precipitates may be mistaken for a Krukenberg spindle on cursory examination.
5. **Subacute angle-closure glaucoma** may be associated with a heavily pigmented trabeculum where the iris root has been in contact with the angle.

Neovascular glaucoma

Introduction

Pathogenesis

Neovascular glaucoma (NVG) is a relatively common and serious condition which occurs as a result of iris neovascularization (rubeosis iridis). The common aetiopatho-

genic factor is severe, diffuse and chronic retinal ischaemia. It is postulated that hypoxic retina produces vasoproliferative growth factors in an attempt to revascularize hypoxic areas. Apart from inducing retinal neovascularization (proliferative retinopathy) such factors also diffuse into the anterior segment and initiate rubeosis iridis and neovascularization in the angle of the anterior chamber. The latter initially impairs aqueous outflow in the presence of an open angle and later contracts to produce a secondary angle-closure glaucoma which is usually severe and relentless. NVG can often be prevented by timely treatment of ischaemic retina by laser photocoagulation.

Causes

1. **Ischaemic central retinal vein occlusion** accounts for 36% of cases. Approximately 50% of eyes develop NVG following ischaemic central retinal vein occlusion. Extensive peripheral retinal capillary non-perfusion on fluorescein angiography is the most valuable predictor of the risk of subsequent NVG, although in some patients non-ischaemic occlusion may subsequently become ischaemic. Glaucoma typically occurs 3 months after the occlusion ('100-day glaucoma') but intervals from 4 weeks to 2 years have been documented.
2. **Diabetes mellitus** accounts for 32% of cases. Patients with long-standing diabetes (10 years or more) with proliferative retinopathy are at particular risk. The risk of glaucoma is decreased by appropriate panretinal photocoagulation and increased by cataract extraction, particularly if the posterior capsule is breached. Frequent review is essential during the first 4 postoperative weeks, which represent the crucial period for the development of rubeosis iridis. Pars plana vitrectomy may also precipitate rubeosis iridis if inadequate laser therapy is applied or tractional retinal detachment remains.
3. **Miscellaneous** causes include carotid obstructive disease, central retinal artery occlusion, intraocular tumours, long-standing retinal detachment and chronic intraocular inflammation.

Classification

Despite a degree of overlap it is convenient to divide NVG into the following three stages:

- Rubeosis iridis.
- Secondary open-angle glaucoma.
- Secondary synechial angle-closure glaucoma.

Rubeosis iridis

Clinical features

- Tiny dilated capillary tufts or red spots develop at the pupillary margin (Fig. 9.83) and may be missed unless the iris is examined carefully under high magnification.
- The new vessels grow radially over the surface of the iris (Fig. 9.84) towards the angle, sometimes joining dilated blood vessels at the collarette. At this stage the IOP may still be normal; and the new vessels may regress spontaneously or with treatment.

Fig. 9.83
Rubeosis iridis on the pupillary border

Fig. 9.84
Moderate rubeosis iridis

NB: Angle neovascularization in the absence of pupillary involvement may occur after central retinal vein occlusion. It is therefore important to perform careful gonioscopy in eyes at high risk even when the pupillary border is uninvolved.

Management

1. **Panretinal photocoagulation**, if performed early, is often effective in inducing regression of the new vessels and preventing subsequent progression to glaucoma.
2. **Retinal surgery.** If rubeosis develops or persists following vitrectomy in a diabetic patient with residual retinal detachment, retinal reattachment should be attempted, and if successful, the rubeosis will frequently regress. Additional panretinal photocoagulation will also be beneficial.

Fig. 9.85
Early angle neovascularization

Secondary open-angle glaucoma

Clinical features

The new blood vessels continue to grow across the iris surface towards the iris root. The neovascular tissue then proliferates across the face of the ciliary body and scleral spur to invade the angle (Fig. 9.85). Here the new blood vessels arborize and form a fibrovascular membrane, which blocks the trabeculum and gives rise to a secondary open-angle glaucoma.

Treatment

1. **Medical** treatment is as for POAG but miotics should be avoided. Topical atropine 1% and intensive topical steroids should be given to reduce inflammation and promote comfort.
2. **Panretinal photocoagulation** should still be performed even if the IOP is adequately controlled medically although this will not influence the fibrous component of the fibrovascular membrane.

Secondary angle-closure glaucoma

This is caused by contraction of fibrovascular tissue in the angle with pulling of the peripheral iris over the trabeculum. The angle thus closes circumferentially in a zipper-like fashion.

Clinical features

- Visual acuity is severely reduced.
- Congestion of the globe and pain.
- Very high IOP and corneal oedema.
- Aqueous flare due to leakage of proteins from the iris new vessels.
- Severe rubeosis iridis (Fig. 9.86) with distortion of the pupil and ectropion uveae due to radial contraction of fibrovascular tissue (Fig. 9.87).

Fig. 9.86
Severe rubeosis iridis (Courtesy of J. Salmon)

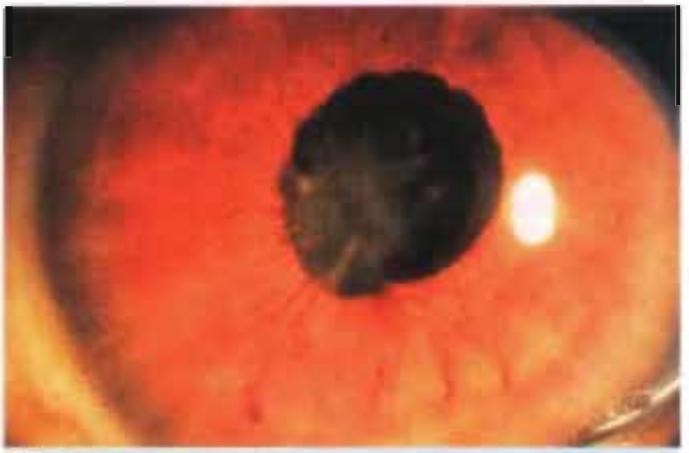

Fig. 9.87
Distortion of the pupil and ectropion uveae in severe rubeosis iridis (Courtesy of J. Salmon)

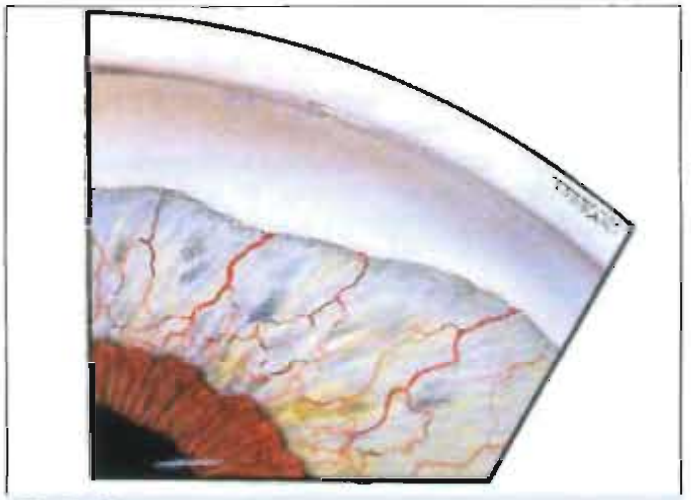

Fig. 9.88
Total synechial angle closure

- Gonioscopy shows synechial angle closure with inability to visualize any angle structures posterior to Schwalbe line (Fig. 9.88).

Treatment

This is aimed mainly at relieving pain, as the prognosis for maintaining visual function is extremely poor.

1. **Medical** treatment is with topical and systemic hypotensive agents except miotics. Topical atropine and steroids may decrease the inflammation and make the eye more comfortable and less congested, even if the IOP remains high.
2. **Retinal ablation** is performed by argon laser, if possible. In eyes with opaque media this can be achieved by trans-scleral diode laser photocoagulation or cryotherapy.
3. **Surgery** may be considered if vision is 'hand movements' or better. The two options are trabeculectomy with adjunctive mitomycin C or artificial filtering shunts.

> *NB:* Although surgery may succeed in lowering IOP, many eyes subsequently lose light perception or become phthisical, so that the main benefit is that of pain relief.

4. **Cyclodestruction** by trans-scleral diode laser may effectively control IOP and render the eye more comfortable, particularly in conjunction with medical therapy.
5. **Retrobulbar alcohol injection** is useful in relieving pain but it may cause permanent ptosis and does not relieve congestion.
6. **Enucleation** if all else fails.

Differential diagnosis

1. **Primary congestive angle-closure glaucoma.** NVG may occasionally present with sudden onset of pain, congestion and corneal oedema. Gonioscopy after clearing the cornea with ocular hypotensive agents and/or topical glycerine is useful to differentiate the two. Moreover, the fellow eye manifests a normal angle.
2. **Postvitrectomy inflammation** in diabetic patients may be associated with congested and prominent iris vasculature and a transient rise in IOP, which may be mistaken for neovascular glaucoma. However, these features usually resolve following the intensive administration of topical steroids.

Inflammatory glaucoma

Introduction

Glaucoma secondary to intraocular inflammation frequently presents a diagnostic and therapeutic challenge. The elevation of IOP may be transient and innocuous, or persistent and severely damaging. Secondary glaucoma is the most common cause of blindness in children and young adults with chronic anterior uveitis.

Classification

1. Angle closure with pupil block.
2. Angle closure without pupil block.
3. Open angle.
4. Specific hypertensive uveitis syndromes.
   - Fuchs uveitis syndrome.
   - Posner–Schlossman syndrome.

Diagnostic problems

1. **Fluctuation of IOP** may be dramatic in uveitic glaucoma and phasing may be helpful in patients with borderline IOP.
2. **Ciliary body shutdown** caused by acute exacerbation of chronic anterior uveitis is frequently associated with lowering of IOP that may mask the underlying tendency to glaucoma. Even eyes with considerably elevated IOP (30–35 mmHg) may become hypotonous during acute exacerbations of uveitis. Return of ciliary body function with subsidence of uveitis may be associated with a rise in IOP in the presence of permanently compromised outflow facility.

> *NB:* It is important to perform gonioscopy in eyes with anterior uveitis and to continue monitoring the IOP as the inflammation resolves.

3. **The mechanisms** of elevation of IOP may be unclear; multiple mechanisms may be involved. Steroid-responders often represent a therapeutic challenge.

Angle-closure glaucoma with pupil block

Pathogenesis

Secondary pupil block glaucoma is caused by posterior synechiae extending for 360° (seclusio pupillae) and obstruct aqueous flow from the posterior to the anterior chamber. The resultant increased pressure in the posterior chamber produces anterior bowing of the peripheral iris (iris bombé), with shallowing of the anterior chamber and apposition of the peripheral iris to the trabeculum and peripheral cornea. Such an inflamed iris easily sticks to the trabeculum; and the iridocorneal contact becomes permanent with the development of peripheral anterior synechiae (PAS).

> *NB:* Angle-closure glaucoma with pupil block is uncommon; most eyes with seclusio pupillae exhibit normal or subnormal IOP due to concomitant chronic ciliary body shutdown.

Clinical features

1. **Slit-lamp biomicroscopy** shows seclusio pupillae, iris bombé and a shallow anterior chamber (Fig. 9.89).

Fig. 9.89
Iris bombé and a very shallow anterior chamber

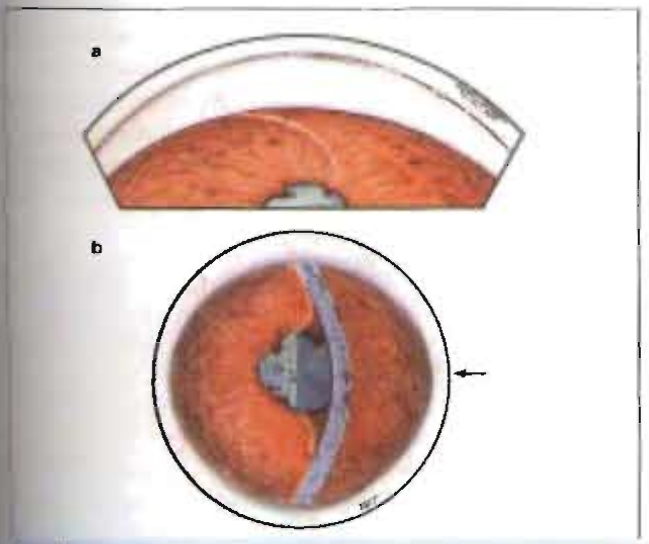

Fig. 9.90
Secondary pupil block angle closure. (a) Gonioscopic view; (b) slit-lamp view

2. **Gonioscopy** shows angle closure from iridotrabecular contact (Fig. 9.90). Indentation gonioscopy with a Zeiss four-mirror goniolens, or equivalent, may be used to assess the extent of appositional as opposed to synechial angle closure.

Treatment

1. **Medical** treatment is initially with topical aqueous suppressants although short-term systemic carbonic anhydrase inhibitors may be required in severe cases.

> The following drugs should be avoided in uveitic glaucoma:
> - Prostaglandin analogues enhance breakdown of the blood–aqueous barrier and may exacerbate cystoid macular oedema. They have rarely been reported to cause acute anterior uveitis.
> - Pilocarpine is also contraindicated because it will promote the development of posterior synechiae.

2. **Laser iridotomy** is performed to re-establish communication between the posterior and anterior chambers. This will eliminate only the element of pupil block and will therefore be effective in lowering IOP only if at least 25% of the angle is still open. Intensive topical steroid therapy may help to minimize post-laser inflammation. It is recommended that several large openings be made and the patient examined at frequent intervals to ensure that they remain patent. Surgical iridectomy may be considered if the laser iridotomy closes.
3. **Trabeculectomy** with adjunctive antimetabolites may be required in eyes with permanent angle closure. Trabeculectomy alone has a high failure rate because patients tend to be young and the conjunctiva has frequently been subjected to chronic exposure to preservatives from steroid and mydriatic drops.
4. **Artificial filtering shunts** may be required in resistant cases.
5. **Cycloablation** when other modalities fail.

Angle-closure glaucoma without pupil block

1. **Pathogenesis.** Chronic anterior uveitis causes the deposition of inflammatory debris in the angle, subsequent organization and contraction of which pulls the peripheral iris over the trabeculum, thereby causing gradual and progressive synechial angle closure (Fig. 9.91) with eventual elevation of IOP. The eye with a pre-existing narrow angle may be at higher risk, as may one with granulomatous inflammation with inflammatory nodules in the angle.
2. **Clinical features.** The anterior chamber is deep but gonioscopy shows extensive angle closure by PAS (Fig. 9.92).
3. **Treatment** is similar to secondary angle-closure glaucoma except that iridectomy is not indicated.

Open-angle glaucoma

In acute anterior uveitis

Here the IOP is usually normal or subnormal due to concomitant ciliary shutdown. Occasionally, however, a

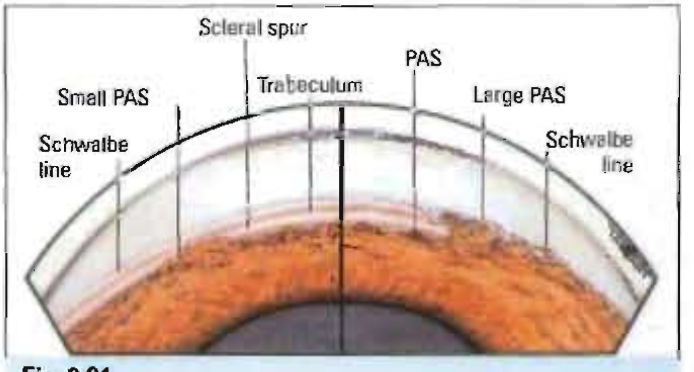

Fig. 9.91
Partial angle closure by peripheral anterior synechiae

Fig. 9.92
Extensive peripheral anterior synechiae

secondary open-angle glaucoma develops due to obstruction of aqueous outflow, most commonly as the acute inflammation is subsiding and ciliary body function is returning. This effect, which is often transient and innocuous, may be steroid-induced or caused by a combination of the following mechanisms:

1. **Trabecular obstruction** by inflammatory cells and debris which may be associated with increased aqueous viscosity due to leakage of proteins from the inflamed iris blood vessels.
2. **Acute trabeculitis** involving inflammation and oedema of the trabecular meshwork with secondary diminution of intertrabecular porosity may result in a reduction in outflow facility. It is thought that this is relevant in anterior uveitis associated with herpes zoster and herpes simplex.
3. **Prostaglandins** may be associated with raised IOP although the exact mechanism is uncertain.

In chronic anterior uveitis

Here the main mechanism for reduced outflow facility is thought to be trabecular scarring and/or sclerosis secondary to chronic trabeculitis. The exact incidence and importance of this mechanism are, however, difficult to determine as most eyes also have some degree of synechial angle closure. Because of the variable appearance of the angle on gonioscopy, definitive diagnosis of trabecular damage is difficult. Theoretically, the angle should be open and, in some eyes, a gelatinous exudate resembling 'mashed potatoes' is seen on the trabeculum. Treatment is as for secondary synechial angle-closure glaucoma.

Glaucoma in Fuchs uveitis syndrome

Fuchs uveitis syndrome (FUS) is an idiopathic, unilateral, chronic, non-granulomatous, anterior uveitis with an insidious onset, which is resistant to steroid therapy (*see* Chapter 10). The most common complication is cataract. Secondary open-angle glaucoma, probably due to trabecular sclerosis, occurs in about 30% of cases; patients must therefore be screened at 6-monthly intervals. Elevation is initially intermittent, later becomes constant. Occasionally the pressure rise may be precipitated by surgery. Treatment is similar to that of other types of uveitic glaucoma.

Posner–Schlossman syndrome

Posner–Schlossman syndrome (glaucomatocyclitic crisis) is characterized by recurrent attacks of unilateral, acute secondary open-angle glaucoma associated with mild anterior uveitis. The cause of the raised IOP is presumed to be acute trabeculitis. This very rare condition typically affects young adults, 40% of whom are positive for HLA-Bw54. Males are affected more frequently than females. The IOP is elevated between a few hours and several days. The attacks are unilateral, although 50% of patients have bilateral involvement at different times. The intervals between attacks vary and, with time, usually become longer. Patients should be followed, even after the attacks have completely subsided, because a significant percentage will develop chronic open-angle glaucoma.

1. **Presentation** is with mild discomfort, halos around lights and slight blurring of vision.
2. **Slit-lamp biomicroscopy** shows corneal epithelial oedema due to a high IOP (40–80 mmHg), a few aqueous cells and fine white central keratic precipitates (Fig. 9.93).
3. **Gonioscopy** shows an open angle. Unless it is performed the condition may be confused with acute primary angle closure glaucoma. The absence of PAS helps in differentiation from other inflammatory glaucomas.
4. **Treatment** is with topical steroids to control inflammation and aqueous suppressants for the raised IOP. Oral non-steroidal anti-inflammatory agents may also be beneficial.

Fig. 9.93
Corneal epithelial oedema and fine keratic precipitates in the Posner–Schlossman syndrome

Lens-related glaucoma

Phacolytic glaucoma

1. **Pathogenesis.** Phacolytic glaucoma (lens protein glaucoma) is a secondary open-angle glaucoma, occurring in association with a hypermature cataract. It is more common in underdeveloped countries where patients with cataract often present late. Trabecular obstruction is caused by high-molecular-weight lens proteins which have leaked through the intact capsule into the aqueous humour. Lens protein-laden macrophages may also contribute to trabecular blockage (Fig. 9.94).

> *NB:* This condition must not be confused with phacoanaphylactic (phacoantigenic) uveitis, which is an autoimmune granulomatous reaction to lens proteins occurring in an eye with a ruptured capsule.

2. **Slit-lamp biomicroscopy**
   - The cornea may be oedematous.

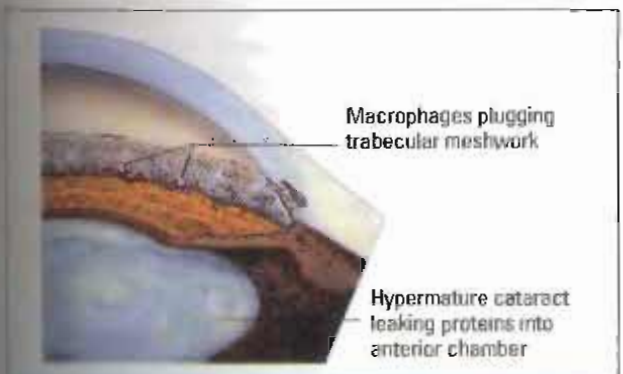

Fig. 9.94
Pathogenesis of phacolytic glaucoma

Fig. 9.95
Hypermature cataract and aqueous particles in phacolytic glaucoma

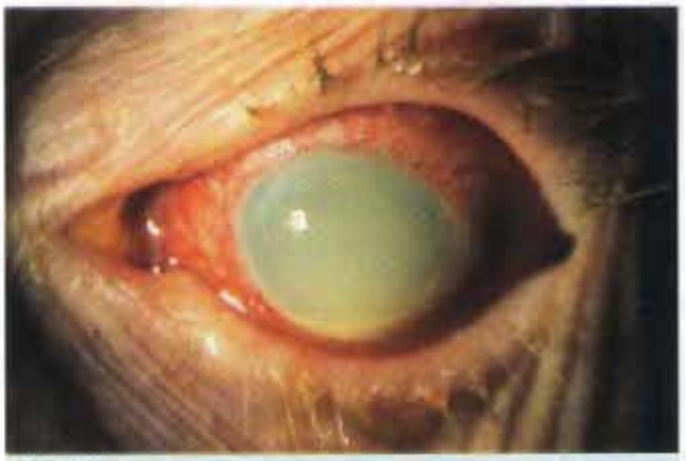

Fig. 9.96
Pseudohypopyon in phacolytic glaucoma

   - The anterior chamber is deep and the aqueous manifests floating white particles (Fig. 9.95), which may form a pseudohypopyon if very dense (Fig. 9.96).
   - A hypermature cataract is seen.
3. **Gonioscopy** shows an open angle.
4. **Treatment**, once the IOP is controlled medically, involves flushing out of proteinaceous material and cataract surgery.

> *NB:* Care must be taken not to rupture the zonules when performing anterior capsulotomy.

Phacomorphic glaucoma

1. **Pathogenesis.** Phacomorphic glaucoma is an acute secondary angle-closure glaucoma precipitated by an intumescent cataractous lens. A history of gradual impairment of vision or an increase in myopia may be obtained. The crystalline lens continues to grow throughout life. Equatorial growth (which slackens the suspensory ligament, thus

Fig. 9.97
Corneal oedema, shallow anterior chamber, dilated pupil and intumescent cataract in phacomorphic glaucoma

allowing the lens to move anteriorly) combines with anteroposterior growth to increase iridolenticular contact and potentiate pupillary block and iris bombe. Phacomorphic glaucoma and PACG therefore conceptually overlap; it may be difficult to distinguish the two in a clinical setting.

2. **Presentation** is similar to acute PACG with a shallow anterior chamber and dilated pupil (Fig. 9.97). A lens opacity is usually evident.

> ***NB:*** Examination of the fellow eye may demonstrate a deep anterior chamber and an open angle, thus excluding the diagnosis of PACG. Axial length measurement and records of the refraction may also be helpful in distinguishing between the two conditions.

3. **Treatment** is initially similar to acute PACG. Laser iridotomy is performed once the IOP is controlled. Cataract surgery is performed once the eye is quiet but is associated with an increased risk of capsular rupture and vitreous loss.

Traumatic glaucoma

Red cell glaucoma

Pathogenesis

A traumatic hyphaema may be associated with elevation of IOP due to trabecular blockage by red blood cells. Pupillary occlusion by a blood clot may superimpose an angle-closure component. Secondary haemorrhage, often more severe than the primary bleed, may develop within 3–5 days of the initial injury, more commonly in black people. Patients with sickle-cell haemoglobinopathies are at increased risk of developing complications associated with traumatic hyphaema.

Risk of glaucoma

Although most traumatic hyphaemas are relatively innocuous and transient, severe and prolonged elevation of IOP may damage the optic nerve and cause blood staining of the cornea. The latter can progress very rapidly and may take years to clear. The optic nerve is endangered by IOP > 50 mmHg for 2 days. The size of a hyphaema is a useful indicator of visual prognosis and risk of complications:

- Hyphaema involving less than half the anterior chamber is associated with a 4% incidence of raised IOP, a 22% incidence of complications and a final visual acuity of >6/18 in 78% of eyes.
- Hyphaema involving more than half the anterior chamber (Fig. 9.98) is associated with an 85% incidence of raised IOP, 78% incidence of complications and a final visual acuity of >6/18 in only 28% of eyes.

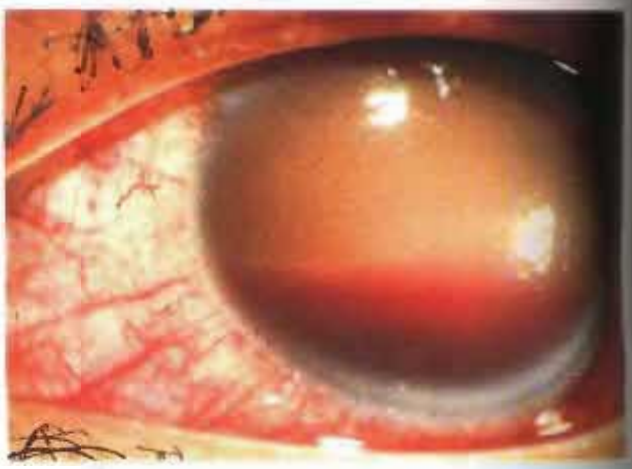

Fig. 9.98
Large hyphaema

Treatment of secondary glaucoma

Hospital admission is required for large hyphaemas.

1. **Medical**
   - Beta-blockers and/or systemic carbonic anhydrase inhibitors depending on the level of IOP. Miotics should be avoided as they may increase pupil block.
   - Topical steroids and mydriatics are useful, since there is often a superimposed element of traumatic anterior uveitis. It is preferable to achieve constant mydriasis rather than a mobile pupil in order to minimize the chances of secondary haemorrhage from the iris or ciliary body.
2. **Surgical evacuation** of the blood with or without trabeculectomy is indicated in the following circumstances:
   - An IOP of >50 mmHg for 2 days or >35 mmHg for 7 days.
   - Early corneal blood staining because it can progress to dense opacity within a few hours.
   - Total hyphaema for more than 5 days to prevent the development of peripheral anterior synechiae and chronic secondary glaucoma.

Angle recession glaucoma

Pathogenesis

Angle recession involves rupture of the face of the ciliary body, the portion that lies between the iris root and the scleral spur, due to blunt trauma, and is detected gonioscopically as an irregular widening of the ciliary body band. Although a large percentage of eyes with traumatic hyphaema exhibit some degree of angle recession, only 6–9% develop glaucoma after 10 years. It is thought that the rise in IOP is secondary to trabecular damage rather than from angle recession itself. However, the risk of glaucoma is directly related to the extent of angle recession. Since glaucoma may not develop until months or even years after the initial injury, angle recession mandates periodic review.

Fig. 9.99
Angle recession with irregular widening of the ciliary body band (Courtesy of J. Salmon)

Clinical features

1. **Presentation** is at any age with unilateral chronic glaucoma. The diagnosis may be easily missed unless a careful past history is taken and gonioscopy performed.
2. **Slit-lamp biomicroscopy** shows signs of previous blunt trauma (see Chapter 19).
3. **Gonioscopy** may show an irregular, scarred and recessed angle with pigment within the recess (Fig. 9.99). In long-standing cases, the cleft may be obscured by fibrosis. On cursory examination, hyperpigmentation in the angle may be mistaken for pigmentary glaucoma, particularly if the corneal endothelium is also covered by pigment granules.

> **NB:** It is important to compare the angle appearance in the two eyes and also to compare different parts of the angle in the same eye.

Treatment

1. **Medical** treatment is as for other types of secondary open-angle glaucoma but is frequently unsatisfactory (laser trabeculoplasty is ineffective).
2. **Trabeculectomy** with adjunctive antimetabolite therapy is the most effective surgical procedure.
3. **An artificial filtering shunt** should be considered if trabeculectomy fails.

Iridocorneal endothelial syndrome

The iridocorneal endothelial (ICE) syndrome typically affects one eye of a young to middle-aged woman. It consists of the following three very rare and frequently overlapping disorders: (a) *progressive iris atrophy*, (b) *iris naevus (Cogan–Reese syndrome)* and (c) *Chandler syndrome*.

Pathogenesis

The common link between the three variants of the ICE syndrome is an abnormal corneal endothelial cell layer which has the capacity to proliferate and migrate across the angle and onto the surface of the iris. The term 'proliferative endotheliopathy' has therefore been suggested to describe this disorder. The ICE syndrome may progress to glaucoma, corneal decompensation or both. Glaucoma is due to synechial angle closure secondary to contraction of this abnormal tissue. Polymerase chain reaction shows the presence of herpes simplex virus DNA in a substantial percentage of ICE syndrome corneal specimens, suggesting that the condition may be of viral origin.

General features

1. Slit-lamp biomicroscopy

- Corectopia (malposition of the pupil) (Fig. 9.100).
- Pseudopolycoria (supernumerary false pupils) in a previously normal iris (Fig. 9.101).
- Iris atrophy of varying severity (Fig. 9.102).

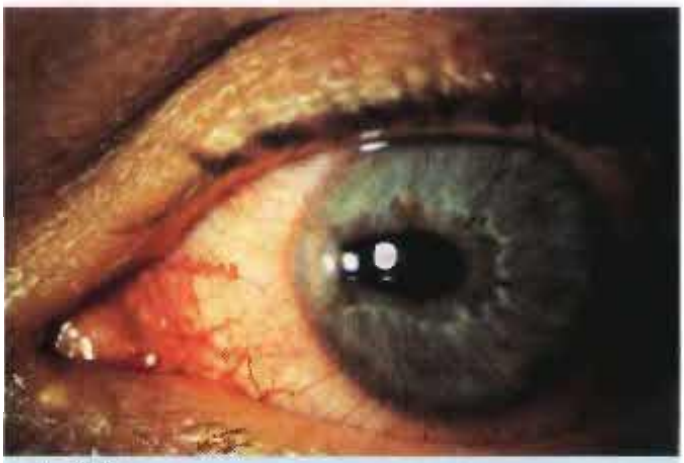

Fig. 9.100
Displacement of the pupil (corectopia) towards the site of peripheral anterior synechiae in ICE

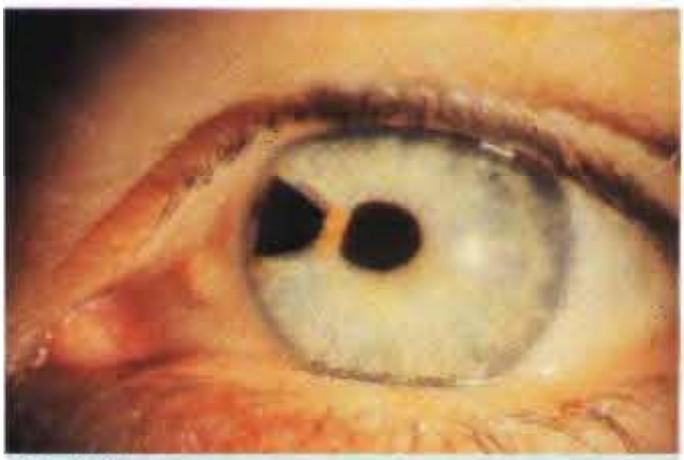

Fig. 9.101
Supernumerary false pupil (pseudopolycoria) in ICE

Fig. 9.102
Stromal iris atrophy in ICE

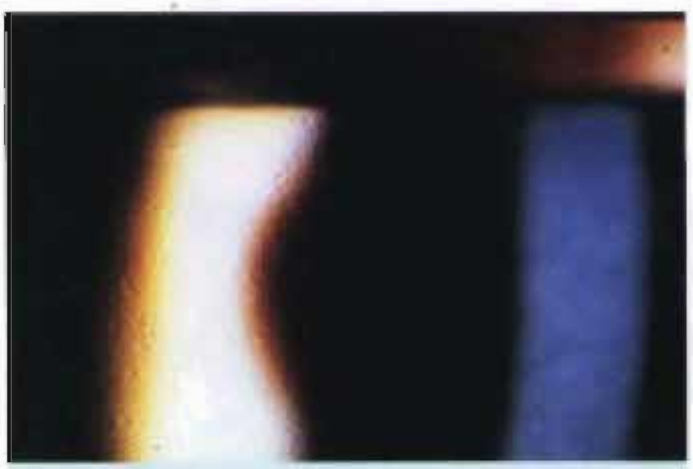

Fig. 9.103
'Hammered-silver' endothelial changes in ICE

Fig. 9.104
Peripheral anterior synechiae in ICE

Fig. 9.105
Progressive iris atrophy

Fig. 9.106
Advanced progressive iris atrophy

Fig. 9.107
Pigmented iris nodules in the Cogan–Reese syndrome

- Corneal endothelial abnormalities characterized by a 'hammered-silver' appearance similar to Fuchs dystrophy when viewed in specular reflected light (Fig. 9.103). Corneal oedema secondary to endothelial decompensation is present in more advanced cases.

2. **Gonioscopy** shows broad-based peripheral anterior synechiae that often extend anterior to Schwalbe line (Fig. 9.104).
3. **Glaucoma** is present in about 50% of cases.

Specific features

In their purest form, the three conditions are easily distinguished from each other. However, there is frequently considerable overlap and clear differentiation may be difficult. Occasionally, during follow-up one condition can be observed changing into another. The differentiation depends primarily on the iris changes.

1. **Progressive iris atrophy** is characterized by severe iris changes with stromal atrophy, hole formation and marked displacement of the pupil towards areas of PAS (Figs 9.105 and 9.106). In between areas of atrophy the stroma appears normal.
2. **The iris naevus (Cogan–Reese) syndrome** is characterized by either a diffuse naevus which covers the anterior iris or by pigmented, pedunculated iris nodules (Fig. 9.107). The pattern of the iris surface appears smudged and matted. Iris atrophy is absent in 50% of cases and in the remainder it is usually mild to moderate although corectopia may be severe.

> **NB:** It is important not to misdiagnose a diffuse iris melanoma as the iris naevus syndrome.

3. **Chandler syndrome** is characterized by severe corneal changes and frequently presents with blurred vision and haloes due to corneal oedema. Stromal atrophy is absent in about 60% of cases and in the remainder is variable in its severity; corectopia is mild to moderate. Glaucoma is usually less severe than in the other two syndromes, and at presentation the IOP may be normal.

Treatment of glaucoma

1. **Medical** treatment is often ineffective.
2. **Trabeculectomy**, even when combined with adjunctive antimetabolite therapy, is frequently unsuccessful because of late-onset bleb failure.
3. **Artificial filtering shunts** are eventually required in many cases.

Miscellaneous secondary glaucomas

Ghost cell glaucoma

1. **Pathogenesis.** Ghost cell glaucoma is due to trabecular obstruction by degenerate erythrocytes. About 2 weeks after vitreous haemorrhage, haemoglobin leaks from the erythrocytes, which evolve into 'ghost' cells, which then pass through a defect in the anterior hyaloid face into the anterior chamber. Because their pliability is lost, the cells become trapped within the pores of the trabeculum and obstruct aqueous outflow. Ghost cell glaucoma may occur in the following settings:

Fig. 9.108
Ghost cell glaucoma

- Cataract surgery in the context of pre-existing vitreous haemorrhage.
- Vitreous haemorrhage in an already aphakic or pseudophakic eye.
- When cataract surgery is complicated by a vitreous haemorrhage and hyphaema. The hyphaema clears, but the red cells in the vitreous persist and evolve into ghost cells.

2. **Clinical features**
   - The cornea may be oedematous due to elevated IOP or surgical trauma.
   - The anterior chamber exhibits ghost cells, which may be recognized as reddish-brown or khaki particles in the aqueous (Fig. 9.108). They should not be confused with leucocytes, since this may result in unwarranted therapy for uveitis.
3. **Treatment**
   a. ***Medical*** treatment with aqueous suppressants.
   b. ***Irrigation*** of the anterior chamber with washing out of the ghost cells if medical therapy fails.
   c. ***Pars plana vitrectomy*** may occasionally be required for persistent vitreous haemorrhage.

Glaucoma in carotid–cavernous fistula

An arteriovenous fistula is an abnormal communication between a previously normal vein and an artery. The blood within the affected vein becomes 'arterialized', and the intravenous pressure rises so that venous blood flow may become altered both in rate and direction. The clinical features of an arteriovenous fistula are largely due to these altered vascular dynamics with subsequent reduction of arterial perfusion, ocular hypoxia and venous congestion (*see* Chapter 17).

1. **Pathogenesis of glaucoma**
   - Secondary open-angle glaucoma due to raised episcleral venous pressure, in turn resulting from a generalized increase in orbital venous pressure, is the most common clinical picture. Gonioscopy may show blood in Schlemm canal.

- Neovascular glaucoma as a result of anterior segment ischaemia.
- Secondary angle closure due to congestion of the uveal tract as a result of increased pressure in the vortex veins (*see* later).

2. **Clinical features.** In patients with large carotid–cavernous fistulae, the other features tend to overshadow the elevation of IOP. However, some patients with relatively mild fistulae, particularly of the indirect type (dural shunt), may present with unilateral glaucoma and congestion of the globe, and the possibility of an underlying carotid–cavernous fistula may be overlooked.
3. **Treatment** is aimed at controlling the IOP medically until the shunt resolves or is treated.

Glaucoma in intraocular tumours

Approximately 5% of eyes with intraocular tumours develop a secondary elevation of IOP. Depending on the location of the tumour one or more of the following mechanisms may be responsible:

1. **Trabecular block**
   - Solid tumour invasion in which the trabeculum is directly invaded by neoplastic cells originating from either a primary melanoma or a metastatic tumour of the anterior uvea. Rarely tumour seeding from a retinoblastoma may also invade the trabeculum.
   - Melanomalytic glaucoma may occur in some eyes with iris melanoma; it is due to trabecular blockage by macrophages which have ingested pigment and tumour cells, similar to phacolytic glaucoma.
2. **Secondary angle closure**
   - Neovascular glaucoma is the most common mechanism in eyes with choroidal melanoma or retinoblastoma.
   - Anterior displacement of the iris–lens diaphragm may occur in an eye with a ciliary body melanoma or a large tumour of the posterior segment.

Glaucoma in ciliochoroidal detachment

1. **Pathogenesis of glaucoma.** Ciliary body detachment with forward rotation around the scleral spur leads to anterior displacement of the iris–lens diaphragm. The anterior chamber shallows, resulting in appositional angle closure without iris bombé.
2. **Causes of ciliochoroidal detachment**
   a. Postoperative
   - Choroidal congestion from an over-tight scleral buckle for retinal detachment.
   - Aggressive panretinal photocoagulation causing inflammatory choroidal exudation.
   - Suprachoroidal haemorrhage following intraocular surgery.
   - After trabeculectomy, especially if there is bleb leakage. The globe is initially hypotonous; later the IOP starts to rise.

   b. Inflammatory causes include scleritis and Harada disease.
   c. Vascular causes include arteriovenous malformation, nanophthalmos and after central retinal vein occlusion.
   d. Uveal effusion syndrome
3. **Signs**
   - Extremely shallow anterior chamber, which is flat peripherally, but without iris bombé.
   - Closed angle.
   - Choroidal detachment.
4. **Treatment**
   a. Medical treatment with mydriatics, topical steroids and aqueous suppressants.
   b. Laser peripheral iridoplasty (gonioplasty), not iridotomy.
   c. Surgery involves repairing a leaking trabeculectomy bleb, cutting an over-tight encircling band and, as a last resort, drainage of choroidal detachment.

Glaucoma in epithelial ingrowth

1. **Pathogenesis.** Epithelial ingrowth is a rare complication of anterior segment surgery or trauma. Conjunctival or corneal epithelial cells migrate through the wound and proliferate in the anterior segment, in a cystic or diffuse manner. The latter is characterized by the proliferation of sheets of epithelial cells over the posterior cornea, trabeculum, iris and ciliary body, and is more commonly associated with secondary glaucoma than the cystic variety. Elevation of IOP is a combination of often pre-existing peripheral anterior synechiae, destruction of the trabeculum by the epithelial membrane and/or obstruction of the trabeculum by desquamated epithelial cells and associated inflammatory cells.
2. **Clinical features**
   - Persistent postoperative anterior uveitis.
   - Diffuse epithelialization is characterized by a translucent membrane with scalloped border involving the posterior corneal surface (Fig. 9.109) and anterior vitreous face in the sector of the incision.
   - Pupillary distortion.

Fig. 9.109
Diffuse epithelial ingrowth

3. **Treatment** of this potentially blinding condition is aimed at eradicating the invading epithelium to avoid recurrence or the conversion of epithelial cysts into diffuse epithelialization with consequent intractable glaucoma.
   a. ***Block excision*** involves simultaneous excision of adjacent iris, pars plicata of the ciliary body, together with all layers of the sclera and cornea in contact with the lesion. The resultant defect is covered with a tectonic corneoscleral graft. The area of iris involvement may be identified by applying argon laser burns which will cause whitening of the affected area.
   b. ***Cryotherapy*** may be applied trans-sclerally to devitalize the epithelium remaining on the posterior surface of the cornea, in the angle and on the ciliary body. Intraocular air is used to insulate other tissues from the effects of the cryotherapy.
   c. ***Artificial filtering shunts*** are of value for medically uncontrolled glaucoma associated with extensive epithelial ingrowth unsuitable for surgical excision.

Glaucoma in iridoschisis

Iridoschisis is a rare condition which typically affects the elderly and is often bilateral. It is associated with underlying angle-closure glaucoma in 90% of cases. It is thought that acute or intermittent angle closure results in iris atrophy because of high IOP.

Fig. 9.110
Shallow anterior chamber in iridoschisis

Fig. 9.111
Mild iridoschisis

Fig. 9.112
Splitting of the anterior leaf of the iris in iridoschisis

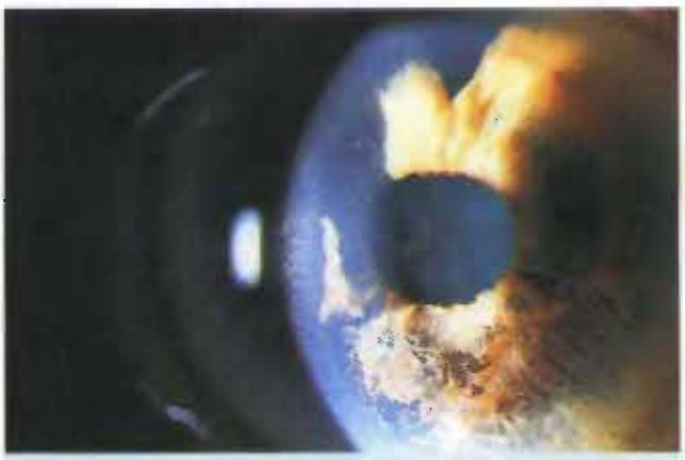

Fig. 9.113
Severe iridoschisis with disintegration of iris fibrils

1. Clinical features

- Shallow anterior chamber (Fig. 9.110).
- Iridoschisis usually involves the inferior iris. The severity ranges from intrastromal atrophy (Fig. 9.111) to extensive splitting of the anterior leaf (Fig. 9.112) and disintegrated iris fibrils (Fig. 9.113) which may float in the anterior chamber.
- Gonioscopy shows a narrow occludable angle which may be associated with peripheral anterior synechiae.

2. **Treatment** initially involves peripheral laser iridotomy. Subsequent treatment is aimed at limiting glaucomatous damage.

Primary congenital glaucoma

Although primary congenital glaucoma (PCG) is the most common of the congenital glaucomas, it is still a very rare condition, affecting 1:10,000 births; 65% of patients are boys.

Most cases of PCG are sporadic. In approximately 10% inheritance is autosomal recessive with incomplete penetrance.

Pathogenesis

Impaired aqueous outflow in PCG is caused by maldevelopment of the angle of the anterior chamber, unassociated with any other major ocular anomalies (isolated trabeculodysgenesis). Clinically, trabeculodysgenesis is characterized by absence of the angle recess with the iris inserted directly into the surface of the trabeculum in one of two configurations:

1. **Flat iris insertion**. The iris inserts flatly and abruptly into the thickened trabeculum at or anterior to the scleral spur (Fig. 9.114a).
2. **Concave iris insertion** is less common. The superficial iris tissue sweeps over the iridotrabecular junction and the trabeculum (Fig. 9.114b). In contrast to a flat iris insertion, the angular structures are obscured by the overlying iris tissue, which is either sheet-like or consists of a dense arborizing meshwork.

Classification

1. **True congenital glaucoma** (40%) in which IOP becomes elevated during intrauterine life.
2. **Infantile glaucoma** (55% of cases) which manifests prior to the third birthday.
3. **Juvenile glaucoma**, the least common, in which the pressure rise develops after the third birthday but before the age of 16 years. This condition may simulate POAG. Gonioscopy is normal or reveals trabeculodysgenesis.

Clinical features

These depend on the age of onset and the level of IOP. Both eyes are affected in 75% of cases although involvement is frequently asymmetrical.

1. **Corneal haze** is often the first sign noticed by the parents (Fig. 9.115). It is caused by epithelial and stromal oedema secondary to raised IOP and may be associated with lacrimation, photophobia and blepharospasm.
2. **Buphthalmos** is a large eye as a result of stretching due to elevated IOP prior to the age of 3 years (Fig. 9.116). It is not usually reported by the parents unless unilateral and advanced. As the sclera stretches it becomes thinner and translucent; the eye then takes on a blue appearance due to enhanced visualization of the underlying uvea. As ocular enlargement continues the anterior chamber deepens; in advanced cases, the zonular fibres stretch and the lens may rarely subluxate. The increased axial length also causes axial myopia, which may give rise to anisometropic amblyopia.

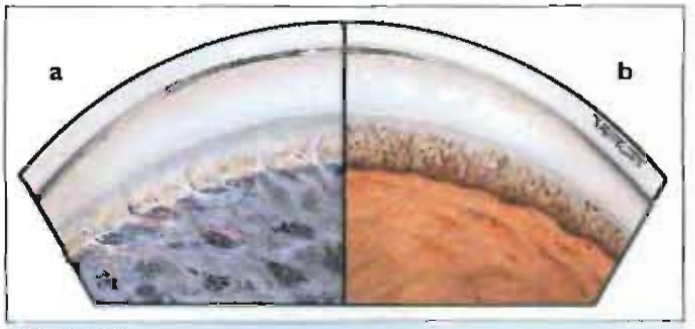

Fig. 9.114
Trabeculodysgenesis in primary congenital glaucoma. (a) Flat anterior iris insertion; (b) concave iris insertion

Fig. 9.116
Bilateral buphthalmos involving the right eye more than the left

Fig. 9.115
Cloudy cornea in congenital glaucoma

Fig. 9.117
Haab striae

3. **Breaks in Descemet membrane** (Fig. 9.117) secondary to corneal stretching may be associated with a sudden influx of aqueous into the corneal stroma. Chronic stromal oedema may lead to permanent scarring. Haab striae represent healed breaks in Descemet membrane and appear as horizontal curvilinear lines.
4. **Optic disc cupping** in infants may regress once the IOP is normalized. Most normal infants exhibit no apparent cup; very few have a cup–disc ratio greater than 0.3, unlike a high percentage of infants with PCG. In contrast to the adult eye, the scleral canal in the infant eye enlarges as part of the generalized enlargement of the globe and the lamina cribrosa may bow posteriorly, in response to elevated IOP. Cup size may therefore be increased from neuronal loss, enlargement of the scleral canal, or both.

Differential diagnosis

1. **Cloudy cornea at birth**
   - Birth trauma may give rise to corneal oedema due to breaks in Descemet membrane.
   - Intrauterine rubella may give rise to a cloudy cornea due to keratitis.

> **NB:** Ten per cent of infants with the rubella syndrome also have congenital glaucoma due to an angle anomaly similar to that in PCG. This may be missed because the eye may not appear significantly enlarged, due to pre-existing microphthalmos.

   - Metabolic disorders such as mucopolysaccharidoses and mucolipidoses.
   - Congenital hereditary endothelial dystrophy (*see* Chapter 5).
2. **Large cornea** due to megalocornea or very high myopia.
3. **Lacrimation** resulting from delayed canalization of the nasolacrimal duct.
4. **Secondary infantile glaucoma**
   - Tumours such as retinoblastoma and juvenile xanthogranuloma.
   - Persistent hyperplastic primary vitreous.
   - Retinopathy of prematurity.
   - Intraocular inflammation.
   - Trauma.
   - Ectopia lentis.

Initial evaluation

This should be performed under general anaesthesia with intravenous ketamine, since other agents may lower IOP. Examination of the optic discs should be undertaken first, followed by measurement of IOP and corneal diameters, and finally gonioscopy.

1. **The IOP** is measured with the Perkins tonometer or Tono-Pen.
2. **The corneal diameter** is measured in both vertical and horizontal meridians with callipers. A diameter > 11 mm prior to the age of 1 year or > 13 mm at any age should be viewed with suspicion. Diameters of 14 mm are typical of advanced buphthalmos.
3. **Gonioscopy** should be performed with a Koeppe lens or one of the other direct goniolenses.

Surgery

1. **Goniotomy** (Fig. 9.118) is performed at the initial examination if the diagnosis is confirmed, provided there is sufficient corneal clarity and the angle can be visualized. Although this procedure may need to be repeated the eventual success rate is about 85%. Goniotomy is unlikely to

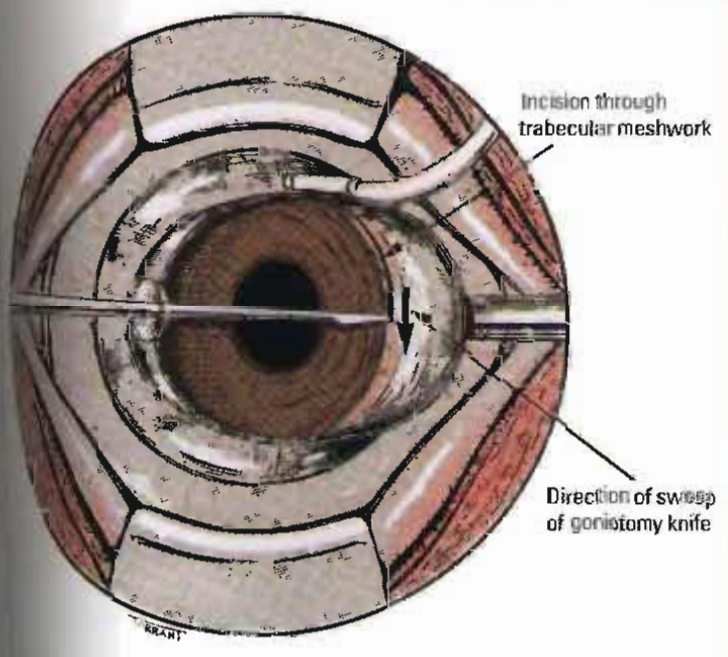

Fig. 9.118
Goniotomy. A circumferential incision is made in the trabecular meshwork

Fig. 9.119
Trabeculotomy. A trabeculotome is inserted into Schlemm canal and rotated into the anterior chamber

be effective if corneal diameter equals or exceeds 14 mm, since in such eyes the canal of Schlemm is obliterated.

2. **Trabeculotomy** (Fig. 9.119) may be necessary if corneal clouding prevents visualization of the angle or when repeated goniotomy has failed.
3. **Trabeculectomy** is often successful, particularly when combined with trabeculotomy and adjunctive antimetabolites.

Follow-up

Patients should be reviewed 1 month after initial surgery. The IOP and corneal diameters should be monitored at regular intervals because progressive enlargement of the corneal diameter is as important a sign of uncontrolled congenital glaucoma as progressive visual field loss in adult glaucoma. About 50% of patients suffer visual loss from optic nerve damage, anisometropic amblyopia, corneal scarring, cataract and lens subluxation. A buphthalmic eye is also susceptible to traumatic damage.

Iridocorneal dysgenesis

Iridocorneal dysgenesis consists of the following overlapping rare congenital disorders involving the cornea and iris, some of which may be associated with glaucoma. These conditions occur as a result of abnormal neural crest cell development and are: (a) *Axenfeld–Rieger syndrome*, (b) *Peters anomaly* and (c) *aniridia*.

Axenfeld–Rieger syndrome

Axenfeld–Rieger syndrome is a spectrum of rare developmental disorders, designated in current nomenclature by the following eponyms:

Axenfeld anomaly

1. **Gonioscopy** shows a prominent and anteriorly displaced Schwalbe line (posterior embryotoxon) (Fig. 9.120) onto which are attached strands of peripheral iris tissue (Fig. 9.121).
2. **Glaucoma** is rare.

Rieger anomaly

This is an AD condition with a high degree of penetrance. Involvement is usually bilateral but not always symmetrical.

Fig. 9.120
Posterior embryotoxon, most marked temporally where Descemet membrane is partially detached

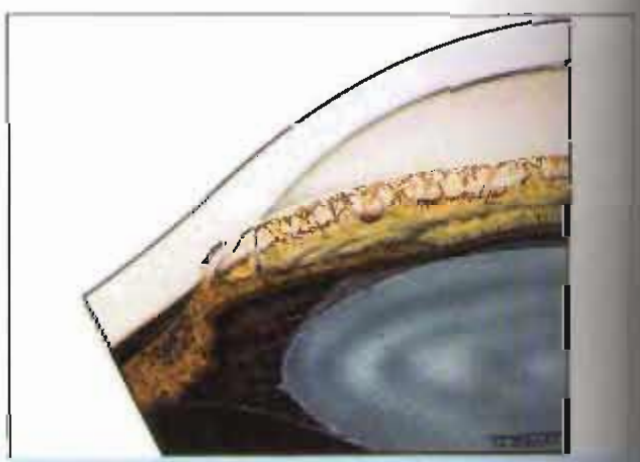

Fig. 9.121
Gonioscopic appearance of Axenfeld anomaly showing strands of peripheral iris attached to a posterior embryotoxon

1. **Slit-lamp biomicroscopy**
   - Posterior embryotoxon.
   - Schwalbe line may become detached into the anterior chamber.
   - Iris stromal hypoplasia (Fig. 9.122), corectopia (Fig. 9.123), pseudopolycoria (Fig. 9.124) and ectropion uveae (Fig. 9.125).
2. **Gonioscopy** in mild cases shows Axenfeld anomaly. In severe cases, broad leaves of the iris stroma adhere to the cornea anterior to Schwalbe line (Fig. 9.126).
3. **Glaucoma** develops in about 50% of cases, usually during early childhood or early adulthood, due to an associated angle anomaly or secondary synechial angle closure. The elevation of IOP should be initially managed medically, although surgery may be required.

Rieger syndrome

This is linked to the region of the epidermal growth factor gene on chromosome 4. It is characterized by Rieger anomaly in association with the following extraocular malformations:

Fig. 9.122
Stromal iris hypoplasia in Rieger anomaly

Fig. 9.123
Corectopia and stromal iris hypoplasia in Rieger anomaly

Fig. 9.124
Corectopia and full-thickness iris defects in Rieger anomaly

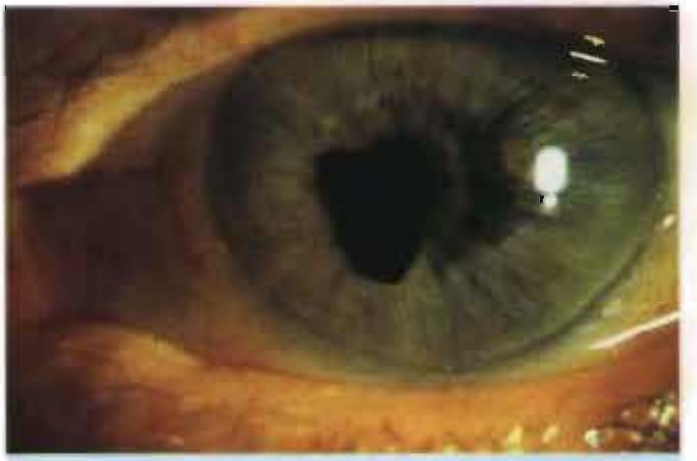

Fig. 9.125
Ectropion uveae and mild iris stromal atrophy in Rieger anomaly

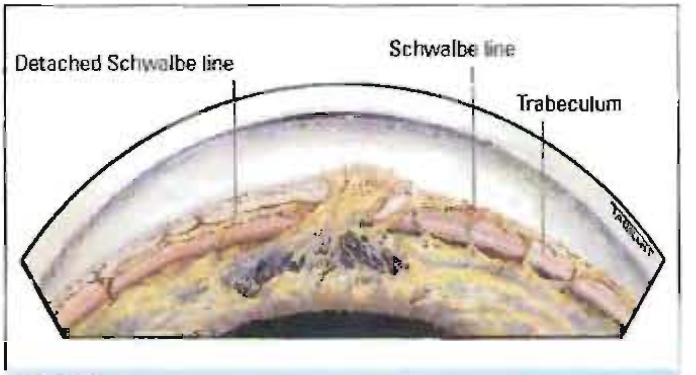

Fig. 9.126
Peripheral anterior synechiae and partial detachment of Descemet membrane in Rieger syndrome

1. **Dental** anomalies consisting of hypodontia (few teeth) and microdontia (small teeth) (Fig. 9.127).
2. **Facial** anomalies include maxillary hypoplasia, broad nasal bridge, telecanthus (increased distance between the medial canthi) and hypertelorism (increased interorbital distance).

Fig. 9.127
Dental abnormalities in Rieger syndrome (Courtesy of K. Nischal)

Fig. 9.128
Redundant paraumbilical skin in Rieger syndrome (Courtesy of K. Nischal)

3. **Other** anomalies include redundant paraumbilical skin (Fig. 9.128) and defects in the region of the pituitary gland.

Peters anomaly

This is an extremely rare but serious condition which is bilateral in 80% of cases. It is the result of defective neural crest cell migration in the sixth to eight weeks of fetal development, during which time the anterior segment of the eye is formed. Most cases are sporadic, although autosomal recessive inheritance and chromosomal defects have been described.

Fig. 9.129
Corneal opacity in Peters anomaly

1. Clinical features

- Corneal opacity (Fig. 9.129) of variable density, without underlying defect involving the posterior stroma, Descemet membrane and endothelium.
- Strands of iris tissue adhere to the margin of the opacity (Figs 9.130 and 9.131a).
- In its more severe degrees the anomaly is characterised by keratolenticular adhesion (Fig. 9.132) or apposition (*see* Fig. 9.131b).

Fig. 9.130
Iridocorneal adhesions in Peters anomaly

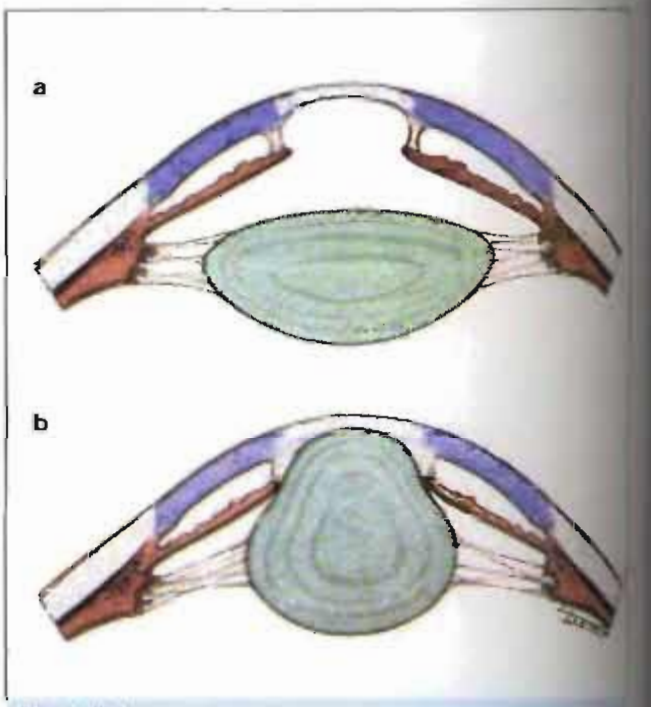

Fig. 9.131
Peters anomaly. **(a)** Iridocorneal adhesions; **(b)** keratolenticular apposition

Fig. 9.132
Keratolenticular adhesion in Peters anomaly

- Miscellaneous occasional anomalies include microphthalmos, cornea plana, sclerocornea, corectopia, iris hypoplasia and anterior polar cataract.

2. **Glaucoma**, which is often congenital, occurs in about 30% of cases as a result of an associated angle anomaly.

Aniridia

Aniridia (AN) is a bilateral condition with life-threatening associations. It occurs as a result of abnormal neuroectodermal development secondary to a mutation in the *PAX6* gene linked to 11p13. This gene controls the development of a number of structures, hence the broad nature of ocular and systemic manifestations. Glaucoma is common and difficult to control.

Classification

1. **AN-1** is AD, accounts for 66% of cases and has no systemic implications. Penetrance is complete, but expressivity variable.
2. **AN-2** (Miller syndrome) is sporadic and accounts for 33%. It carries a 30% risk of Wilm tumour developing before the age of 5 years.
3. **AN-3** (Gillespie syndrome) is recessively inherited and accounts for the remainder. It is associated with mental handicap and cerebellar ataxia.

Clinical features

1. **Presentation** is typically at birth with nystagmus and photophobia. The parents may have noticed absence of iris or dilated pupils.
2. **Signs**
   - *Aniridia* is variable in severity, ranging from minimal (detectable only by retroillumination), to partial (Fig. 9.133) and total (Fig. 9.134). However, even eyes with 'total' involvement usually show a residual frill of iris tissue in the angle on gonioscopy (Fig. 9.135).

Fig. 9.133
Partial aniridia

Fig. 9.134
Total aniridia

Fig. 9.135
Gonioscopic view of aniridia showing remnants of the iris root

   - *Corneal* lesions include opacity, epibulbar dermoids, microcornea, sclerocornea and keratolenticular adhesions. The corneal surface often manifests epithelial

Fig. 9.136
Subluxation of a cataractous lens in aniridia

Fig. 9.137
Episcleral angioma in Sturge–Weber syndrome

defects and may become conjunctivalized as a result of limbal stem cell deficiency.

*c. **Lenticular*** changes include cataract, subluxation (usually superiorly) (Fig. 9.136), congenital aphakia and persistent pupillary membranes.

*d. **Fundus*** may exhibit foveal hypoplasia, optic disc hypoplasia and choroidal coloboma.

Management

1. **Opaque contact lenses** may be used to create an artificial pupil and improve vision and cosmesis.
2. **Topical lubricants** are frequently required for associated keratopathy.
3. **Cataract surgery** is often required. Care must be taken to minimize trauma to the limbus and preserve stem cell function.

Glaucoma

This occurs in approximately 75% of patients and usually presents in late childhood or adolescence.

1. **The mechanism** is synechial angle closure secondary to the pulling forward of rudimentary iris tissue by contraction of pre-existing fibres that bridge the angle.
2. **Treatment** is difficult and the prognosis guarded.
   *a. **Medical*** therapy is inadequate in most cases.
   *b. **Goniotomy*** may prevent subsequent rise in IOP if performed before the development of irreversible synechial angle closure.
   *c. **Artificial filtering shunts*** may be effective in established cases.
   *d. **Diode laser cycloablation*** may be necessary if other modalities fail.

Glaucoma in phacomatoses

Sturge–Weber syndrome

Sturge–Weber syndrome (encephalotrigeminal angiomatosis) is characterized by naevus flammeus and intracranial leptomeningeal angiomata (*see* Chapter 20). Glaucoma develops in about 30% of patients ipsilateral to the facial haemangioma, especially if the lesion affects the upper eyelid.

1. **The pathogenesis** of glaucoma is controversial. Isolated trabeculodysgenesis may be instrumental in the infant, whereas raised episcleral venous pressure associated with an arteriovenous communication in an episcleral angioma (Fig. 9.137) may be responsible in older patients. Often, however, the cause is obscure.
2. **Presentation** of glaucoma in 60% of patients is within the first 2 years of life with buphthalmos. The remainder manifest at any time from infancy to adulthood.
3. **Treatment**
   *a. **Medical*** treatment with topical latanoprost may be successful.
   *b. **Goniotomy*** may be successful in eyes with angle anomalies.
   *c. **Combined trabeculotomy–trabeculectomy*** gives good results in early-onset cases. The rationale is that trabeculotomy addresses the barrier to aqueous outflow imposed by a congenital angle anomaly, while trabeculectomy bypasses the episcleral veins.

> ***NB:*** Surgery carries a high risk of choroidal effusion and suprachoroidal haemorrhage.

Neurofibromatosis-1

Neurofibromatosis-1 (NF-1, von Recklinghausen disease) is a disorder that primarily affects neural cell growth. Inheritance is autosomal dominant with irregular penetrance and variable expressivity (*see* Chapter 20). Glaucoma is uncommon, usually unilateral and congenital. About 5%

Fig. 9.138
Congenital ectropion uveae in neurofibromatosis-1

patients with glaucoma have an ipsilateral neurofibroma of the upper eyelid or exhibit facial hemiatrophy.

Pathogenesis

- Obstruction of aqueous outflow by neurofibromatous tissue in the angle.
- Developmental angle anomaly which may be associated with congenital ectropion uveae (Fig. 9.138).
- Secondary angle closure caused by forward displacement of the peripheral iris associated with neurofibromatous thickening of the ciliary body.
- Secondary synechial angle closure caused by contraction of a fibrovascular membrane.

Treatment is similar to that of primary congenital glaucoma but the prognosis is worse.

Anti-glaucoma drugs

Beta-blockers

Pharmacology

Adrenergic neurones secrete noradrenaline at sympathetic post-ganglionic nerve endings.

1. **Adrenergic receptors** are of the following four main types (Fig. 9.139):
   a. ***Alpha-1*** receptors are located in the arterioles, dilator pupillae and Muller muscle. Stimulation gives rise to hypertension, mydriasis and lid retraction.
   b. ***Alpha-2*** receptors are inhibitory receptors located in the ciliary epithelium. Stimulation results in diminished aqueous secretion. There may also be an increase in uveoscleral outflow.
   c. ***Beta-1*** receptors are located in heart muscle and give rise to tachycardia when stimulated.
   d. ***Beta-2*** receptors are located in the bronchi and ciliary epithelium ($\beta_2 > \beta_1$). Stimulation results in bronchodilation and increased aqueous production.
2. **Beta-blockers** antagonize the effects of catecholamines at beta receptors. They reduce IOP by decreasing aqueous secretion and are therefore useful in all types of glaucoma but about 10% of the population are unresponsive. Beta-blockers may be non-selective or cardioselective. Non-selective beta-blockers are equipotent at beta-1 and beta-2 receptors, while cardioselective are more potent at beta-1 receptors. The advantage, at least in theory, is that the bronchoconstrictive effect of beta-2 blockade is

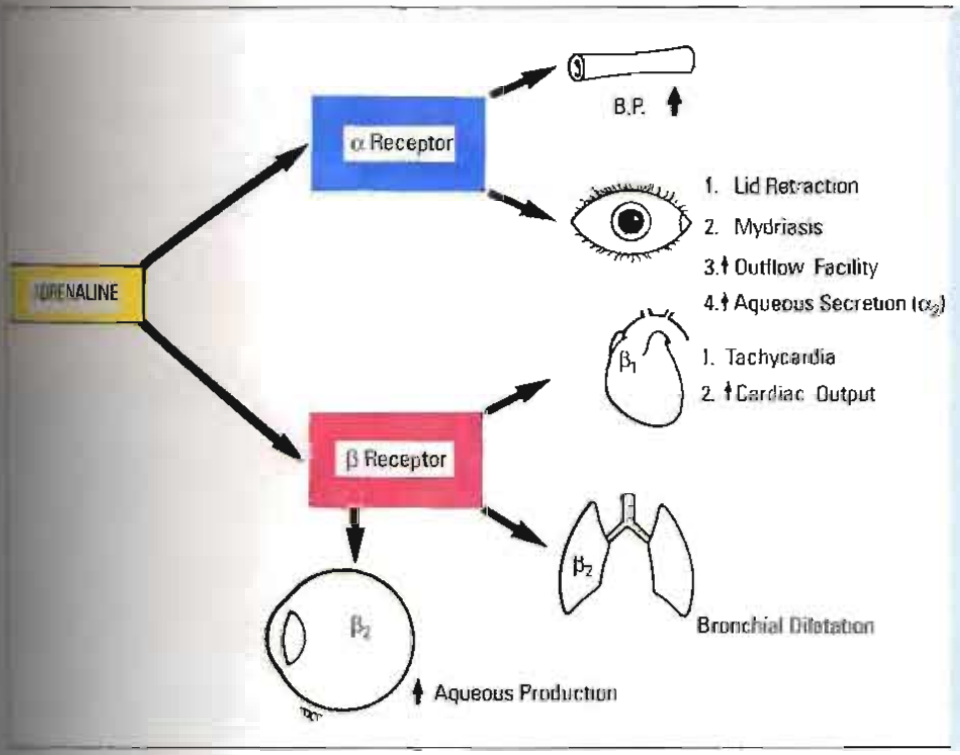

Fig. 9.139
Pharmacology of adrenergic neurones

minimized. Betaxolol is the only cardioselective agent currently available for the treatment of glaucoma. Contraindications to beta-blockers include congestive cardiac failure, second or third degree heart block, bradycardia, asthma and obstructive airways disease.

Timolol

1. **Preparations**
   - Timoptol 0.25%, 0.5% b.d.
   - Timoptol-LA 0.25%, 0.5% once daily.
   - Nyogel-LA 0.1% once daily.
2. **Ocular side effects** include occasional allergy, corneal punctate epithelial erosions and reduced aqueous tear secretion.
3. **Systemic side effects** tend to occur during the first week of administration. Although uncommon they may be serious.
   - Bradycardia and hypotension can result from beta-1 blockade. Beta-blockers are therefore contraindicated in patients with bradycardia and congestive cardiac failure.

> ***NB:*** The patient's pulse must be palpated before prescribing a beta-blocker.

   - Bronchospasm may be induced by beta-2 blockade and may be fatal in pre-existing asthma or severe chronic pulmonary obstruction.
   - Miscellaneous side effects include sleep disorders, hallucinations, confusion, depression, fatigue, headache, nausea, dizziness, decreased libido and possible reduction of plasma high-density lipoprotein level.
4. **Reduction of systemic drug absorption** may be achieved by:
   - Lacrimal occlusion following instillation, by closing the eyes and applying digital pressure over the lacrimal sac area for about 3 minutes. Apart from obstructing lacrimal drainage and reducing systemic absorption, this also prolongs eye–drug contact and increases therapeutic efficacy.
   - Merely closing the eyes for 3 minutes will reduce systemic absorption by about 50%.

Other beta-blockers

1. **Betaxolol** (Betoptic) 0.5% b.d. Although the ocular hypotensive effect is less than timolol, the effect on preservation of the visual field appears to be superior. Betaxolol may increase retinal blood flow by increasing perfusion pressure.
2. **Levobunolol** (Betagan) 0.5% is as potent as timolol. Once-daily administration is often adequate.
3. **Carteolol** (Teoptic) 1%, 2% is similar to timolol but also exhibits intrinsic sympathomimetic activity. It has a more selective action on the eye than on the cardiopulmonary system and may therefore induce less bradycardia than timolol.
4. **Metipranolol** 0.1%, 0.3% b.d. is similar to timolol, but is available only in preservative-free units. It is therefore useful in patients allergic to preservatives or wearing soft contact lenses (in whom benzalkonium chloride should be avoided). It may rarely cause anterior uveitis.

Alpha-2 agonists

These agents decrease IOP by both decreasing aqueous secretion and enhancing uveoscleral outflow.

1. **Brimonidine** (Alphagan) 0.2% b.d. is a highly selective alpha-2 agonist which also has a neuroprotective effect. Its efficacy is less than timolol but better than betaxolol. It exhibits additivity with beta-blockers. Its main ocular side effect is allergic conjunctivitis that may be delayed for up to a year after commencement of therapy. Systemic side effects include xerostomia, drowsiness and fatigue.
2. **Apraclonidine** (Iopidine) 0.5%, 1% is mainly used after laser surgery on the anterior segment to offset an acute rise in IOP. It is not suitable for long-term use because of tachyphylaxis (loss of therapeutic effect over time) and a high incidence of local side effects.

Prostaglandin analogues

Prostaglandin analogues reduce IOP by enhancing uveoscleral outflow.

Latanoprost

This is a prostaglandin F2-alpha analogue.

1. **Preparations**. Latanoprost (Xalatan) 0.005% used once daily.
2. **Efficacy** is superior to timolol although a proportion of patients show no response.
3. **Ocular side effects** include conjunctival hyperaemia, eyelash lengthening and hyperpigmentation of lashes (Fig. 9.140) and periorbital skin. Anterior uveitis and cystoid macular oedema may rarely occur in predisposed eyes. The drug should therefore be used with caution in uveitic glaucoma.
4. **Systemic side effects** include occasional headache and upper respiratory tract symptoms.

Other preparations

1. **Travoprost** (Travatan) 0.004% is similar to latanoprost but may have a superior ocular hypotensive effect.
2. **Bimatoprost** (Lumigan) 0.3% is a prostamide. In addition to facilitating uveoscleral outflow, it also potentiates trabecular outflow.

Fig. 9.140
Right iris hyperchromia and hyperpigmentation of lashes due to latanoprost

3. **Unoprostone isopropyl** (Rescula) 0.15% b.d. is not as effective as latanoprost in lowering IOP and is perhaps unsuited for monotherapy. However, it may be used in combination with latanoprost.

Miotics

Mode of action

Miotics are parasympathomimetic drugs that act by stimulating muscarinic receptors in the sphincter pupillae and ciliary body.

1. **In primary open-angle glaucoma** miotics reduce IOP by contraction of the ciliary muscle, which increases the facility of aqueous outflow through the trabecular meshwork.
2. **In primary angle-closure glaucoma** contraction of the sphincter pupillae and the resultant miosis pulls the peripheral iris away from the trabeculum, thus opening the angle. It is often necessary to reduce IOP with systemic medication before miotics can take effect.

Pilocarpine

1. **Preparations**
   - Pilocarpine 1%, 2%, 3%, 4% is used q.i.d. as monotherapy. When used in combination with a beta-blocker, b.d. administration is adequate.
   - Pilocarpine gel (Pilogel) consists of pilocarpine adsorbed on to a plastic gel, instilled once daily at bedtime so that the induced myopia and miosis last only during sleep. The main disadvantage is the development of a diffuse superficial corneal haze in 20% of users, although this rarely affects visual acuity.
2. **Efficacy** is equal to beta-blockers.
3. **Ocular side effects** include miosis, brow ache, myopic shift and exacerbation of symptoms of cataract. Visual field defects appear denser and larger.
4. **Systemic side effects** are insignificant.

Topical carbonic anhydrase inhibitors

The carbonic anhydrase inhibitors (CAIs) are chemically related to the sulphonamides. They lower IOP by inhibiting aqueous secretion.

1. **Dorzolamide** (Trusopt) 2% t.i.d. is similar in efficacy to timolol but inferior to timolol. The main ocular side effect is allergic conjunctivitis.
2. **Brinzolamide** (Azopt) 1% t.i.d. is similar to dorzolamide, but with a lower incidence of local allergy.

Combined topical preparations

Combined preparations with similar ocular hypotensive effect to the sum of the individual components improve convenience and patient compliance. They are also more cost effective. Examples include:

1. **Cosopt** (timolol + dorzolamide) b.d.
2. **Xalacom** (timolol + latanoprost) once daily.
3. **TimPilo** (timolol + pilocarpine) b.d.

Systemic carbonic anhydrase inhibitors

Systemically administered CAIs are useful as short-term treatment; their long-term use is usually reserved for patients at high risk of visual loss.

Preparations

1. **Acetazolamide tablets** 250 mg. The dose is 250–1000 mg in divided doses. The onset of action is within 1 hour, with a peak at 4 hours and a duration up to 12 hours.
2. **Acetazolamide sustained-release capsules** 250 mg. The dose is 250–500 mg daily with a duration of up to 24 hours.
3. **Acetazolamide powder** 500 mg vials for injection. The onset of action is almost immediate, with a peak at 30 minutes and a duration of up to 4 hours. This is the only CAI preparation available for injection and is useful in acute angle-closure glaucoma.
4. **Dichlorphenamide tablets** 50 mg. The dose is 50–100 mg (2–3 times daily). The onset of action is within 1 hour, with a peak at 3 hours and a duration of up to 12 hours.
5. **Methazolamide tablets** 50 mg. The dose is 50–100 mg (2–3 times daily). The onset of action is within 3 hours, with a peak at 6 hours and a duration of up to 10–18 hours. This is a useful alternative to acetazolamide with a longer duration of action but is currently not available in the United Kingdom.

Systemic side effects

Long-term use of systemic CAIs is frequently limited by systemic side effects (Fig. 9.141). The patient should always be warned of potential side effects as this decreases anxiety and improves compliance.

1. **Common**
   a. ***Paraesthesiae*** characterized by tingling of the fingers, toes, hands or feet, and occasionally at the mucocutaneous junctions, is a universal finding and usually innocuous. Compliance is suspect if the patient denies this symptom.
   b. ***The malaise complex*** is characterized by a combination of malaise, fatigue, depression, weight loss and decreased libido. A supplemental 2-week course of sodium acetate may often be helpful.
2. **Uncommon**
   a. ***The gastrointestinal complex*** is characterized by gastric irritation, abdominal cramps, diarrhoea and nausea. This can occur independently of the malaise syndrome and is unrelated to any specific changes in blood chemistry.
   b. ***Renal stone formation.***
   c. ***Stevens–Johnson syndrome*** may occur since CAIs are sulphonamide derivatives.

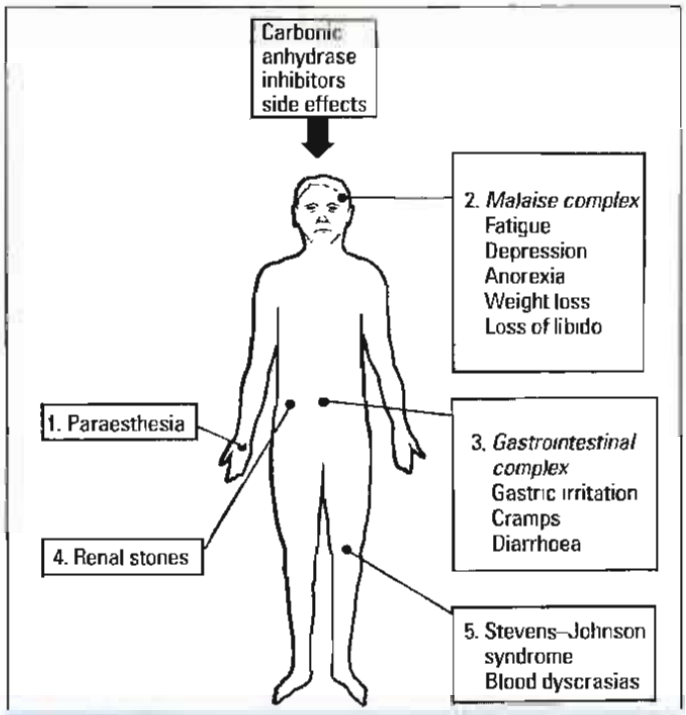

Fig. 9.141
Side effects of systemic carbonic anhydrase inhibitors

*d. **Blood dyscrasias*** are extremely rare and of two types:
- Dose-related bone marrow suppression which usually recovers when treatment is stopped.
- Idiosyncratic aplastic anaemia is not dose-related and has a mortality of 50%. It may occur after only one dose but usually does so during the first 2–3 months and very rarely after 6 months administration.

Hyperosmotic agents

Physiological principles

Osmotic pressure is dependent on the number rather than on the size of solute particles in a solution. Lower molecular weight solutes therefore exert a greater osmotic effect per gram. Hyperosmotic agents remain intravascular, thus increasing blood osmolality. They lower IOP by creating an osmotic gradient between blood and vitreous so that water is 'drawn out' from the vitreous. The higher this gradient the greater the reduction of IOP. To be effective in the eye, a hyperosmotic agent must therefore be unable to penetrate the blood–aqueous barrier. If penetration occurs, an osmotic equilibrium is set up and any further effect is lost. Hyperosmotic agents are therefore of limited value in the treatment of inflammatory glaucomas in which the integrity of the blood–aqueous barrier is compromised.

Clinical uses

When a temporary drop in IOP is required that cannot be obtained by other means.

- In acute angle-closure glaucoma.
- Prior to intraocular surgery when the IOP is very high as may occur from dislocation of the lens into the anterior chamber.

> ***NB:*** These preparations should be given fairly rapidly and the patient should not subsequently be given fluids to quench thirst.

Preparations

1. **Glycerol** is an oral agent with a sweet and sickly taste. Fresh lemon (not orange) juice often needs to be added to avoid nausea. The dose is 1 g/kg body weight or 2 ml/kg body weight (50% solution). Peak action is within 1 hour, with a duration up to 3 hours. Although glycerol is metabolized to glucose, it may be given to well-controlled diabetics.
2. **Isosorbide** is an oral agent with a minty taste. Metabolically inert, it may be given to diabetics without insulin cover. The dose is the same as for glycerol.
3. **Mannitol** is the most widely used intravenous hyperosmotic agent. The dose is 1 g/kg body weight or 5 ml/kg body weight (20% solution in water). Peak action is achieved within 30 minutes, with a duration of up to 6 hours.

Side effects

1. **Cardiovascular overload** may occur as a result of increased extracellular volume. Hyperosmotic agents should therefore be used with great caution in patients with cardiac or renal disease.
2. **Urinary retention** may occur in elderly men following intravenous administration. Catheterization may be necessary in those with prostatism.
3. **Miscellaneous** side effects include headache, backache, nausea and mental confusion.

Laser therapy

Argon laser trabeculoplasty

Argon laser trabeculoplasty (ALT) involves the application of discrete laser burns to the trabeculum. This enhances aqueous outflow and lowers IOP.

Technique

1. A drop of apraclonidine 1% or brimonidine 0.2% is instilled to prevent an early post-laser rise in IOP.
2. Two drops of a topical anaesthetic are instilled.
3. A goniolens is inserted with the mirror at the 12 o'clock position to visualize the inferior angle (usually the easiest part to see).
4. The scleral spur, Schwalbe line (which may be pigmented) and the three-dimensional ground-glass appearance of the trabeculum are identified.

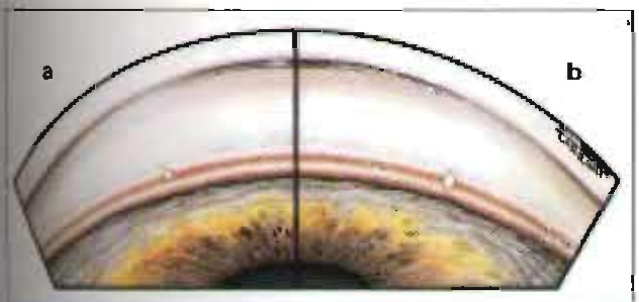

Fig. 9.142
Laser trabeculoplasty. (a) Correct round aiming beam; (b) incorrect oval aiming beam

5. The aiming beam is focused at the junction of the pigmented and non-pigmented trabeculum, ensuring that the spot is round and has a clear edge (Fig. 9.142a). An oval spot with a blurred outline (Fig. 9.142b) means that the aiming beam is not perpendicular to the trabecular surface.
6. Initial laser settings are commonly 50 μm spot size, 0.1 seconds duration and 700 mW power.
7. The laser is fired; the ideal reaction is a transient blanching (Fig. 9.143a) or the appearance of a minute gas bubble (Fig. 9.143b) at the point of incidence. A large gas bubble (Fig. 9.143c) is excessive.
8. If the reaction is inadequate, the power is increased by 200 mW steps. In heavily pigmented angles, a power setting of 400 mW may suffice, whereas a non-pigmented meshwork may require up to 1200 mW (the average is about 900 mW).
9. Twenty-five burns are applied at regularly spaced intervals from one end of the mirror to the other.
10. The goniolens is rotated clockwise by 90° and a further 25 burns applied, making a total of 50 over 180° of the angle. It is important to be familiar with the rotational pattern of the mirror so that adjacent quadrants are treated systematically. With practice it is possible to perform ALT by continuously rotating the goniolens and applying each burn through the centre of the mirror.

NB: Some ophthalmologists initially treat 180° and later treat the other 180° if the response is unsatisfactory. Others, however, treat the entire circumference with 100 burns at the initial sitting.

11. Iopidine 1% or brimonidine 0.2% is instilled.
12. Topical fluorometholone q.i.d. for a week is prescribed; glaucoma medical therapy is continued.

Follow-up

Four to six weeks should be allowed for the treatment to take effect. If the IOP is reduced significantly by 6 weeks, gradual withdrawal of medication may be attempted, although total withdrawal is seldom possible. The main aim of ALT is to obtain a safe IOP; the reduction of medication is usually a secondary consideration. If IOP remains high and only 180° have been treated, the remaining 180° are treated. Following 360° ALT, re-treatment is unlikely to be beneficial and filtration surgery merits consideration.

Complications

1. **Peripheral anterior synechiae** (Fig. 9.143d) may develop if the burns are applied too posteriorly or if the energy level is high. In the majority of cases this does not compromise aqueous outflow.
2. **Small haemorrhages** may develop if the blood vessels on the peripheral iris or ciliary body are inadvertently treated. Such bleeding is easily stopped by applying pressure on the globe with the goniolens.
3. **Acute elevation of IOP** may occur if prophylactic apraclonidine or brimonidine is not used.
4. **Anterior uveitis** is fairly common but usually mild, transient and innocuous.
5. **Adverse effect on subsequent filtration surgery.** The incidence of encapsulated blebs following filtration surgery is up to three times higher in eyes previously treated with ALT.

Results

1. **In POAG** the initial success rate is 75–85%. The average reduction of IOP is about 30%; eyes with initially high IOPs therefore manifest a greater reduction of IOP. Up to 50% of eyes are still controlled after 5 years and about 33% after 10 years. Failure occurs most frequently in the first year; therefore if the IOP is still controlled at 1 year, the probability of control after 5 years is 65% and after 10 years about 40%. If ALT is used as primary treatment,

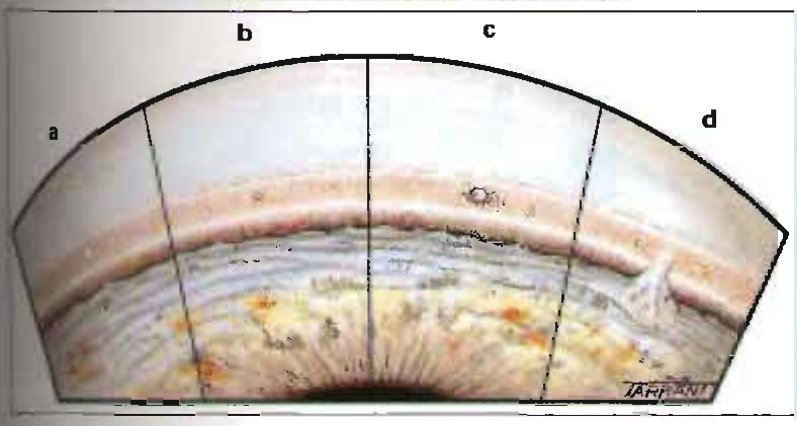

Fig. 9.143
Laser trabeculoplasty. (a) Blanching of the trabeculum: correct reaction; (b) small bubble: also correct reaction; (c) large bubble: excessive reaction; (d) peripheral anterior synechiae: burn applied too posteriorly

50% of cases require additional medical therapy within 2 years. Following initially successful ALT, re-treatment carries a low success rate (30% after 1 year and only 15% after 2 years). In general, the results are less good in patients under the age of 50 years. Black patients respond as well as white initially, but tend to have a more rapid loss of effect.

2. **In normal-tension glaucoma** 50–70% of patients have a good response, but the absolute reduction in IOP is less than in POAG.
3. **In pigmentary glaucoma** results are generally good, though less so in older patients.
4. **In pseudoexfoliation glaucoma** initial results are excellent, although failure may occur earlier than in POAG and subsequent rise in IOP may be rapid.

> ***NB:*** ALT is ineffective in paediatric and most secondary glaucomas with the exception of pigmentary and pseudoexfoliation glaucoma.

Diode laser trabeculoplasty

This gives similar results to ALT, although with less disruption of the blood–aqueous barrier. The following are the main practical differences between the two modalities:

- A higher laser power of 800–1200 mW is used.
- The burns are less intense: although blanching is observed bubble formation does not occur.
- The spot size is 100 μm but can be reduced to 70 μm by using a special contact lens.
- The pulse duration is 0.1 or 0.2 seconds.

Nd:YAG laser iridotomy

Indications

- Primary angle-closure glaucoma: acute, intermittent and chronic.
- Fellow eye of a patient with acute glaucoma.
- Narrow 'occludable' angles.
- Secondary angle closure with pupil block.
- POAG with narrow angles and combined mechanism glaucoma.

Technique

1. A drop of apraclonidine 1% or brimonidine 0.2% is instilled.
2. The pupil should ideally be miosed with topical pilocarpine, although this may not be possible following acute glaucoma.
3. A topical anaesthetic is instilled.
4. A special contact lens such as the Abraham iridotomy lens is inserted (Fig. 9.144).
5. A site is selected, preferably in the superior iris, so that it is covered by the eyelid thus preventing monocular diplopia. The iridotomy should also be as peripheral as possible to minimize damage to the crystalline lens although an arcus senilis may render this difficult. Finding an iris crypt is beneficial but not essential.
6. The beam is angled so that it is non-perpendicular and aimed towards the peripheral retina to avoid the remote possibility of a macular burn.
7. Laser settings vary with different machines. Most iridotomies are made with settings of 4–8 millijoules (mJ). For a thin blue iris the required energy level is 1–4 mJ per shot, with two to three shots per burst. Thick, velvety smooth, brown irides necessitate higher energy levels, which may be achieved with higher power or more shots per burst. Although such higher energy levels and more shots per burst render penetration of the iris easier they carry an increased risk of intraocular damage.

Fig. 9.144
Abraham lens used for laser iridotomy

> ***NB:*** As a general guideline three bursts of 3–6 mJ are usually effective.

8. The beam is focused precisely and the laser fired. Successful penetration is characterized by a gush of pigment debris. On average seven shots are required to produce an adequate iridotomy (Fig. 9.145) although with practice this can be reduced to one or two.
9. A drop of apraclonidine 1% or brimonidine 0.2% is instilled.
10. A strong topical steroid is prescribed every 10 minutes for 30 minutes and then hourly on the day of treatment and then q.i.d. for 1 week.

Potential technical problems

1. **Initial failure** is managed by re-treating the same site, moving to a different site and increasing the energy level. The decision to re-treat the same site depends in part on the degree of pigment dispersion and haemorrhage caused by the previous partial treatment. In thick brown irides, incomplete treatment may result in a thick cloud of dispersed iris pigment which impairs visualization and accurate focusing on the base of the crater. Further applications applied into the cloud often merely increase

Fig. 9.145
Correct size opening in the iris

the pigment and haemorrhage, without producing an opening. In this situation it is best to wait for the cloud to disperse and then re-treat the same site, or to increase the energy level and try a different site. Alternatively a potential site may be pre-treated with an argon laser.

2. **Opening too small.** It is sometimes easier to create an additional opening at a different site rather than to try to enlarge the opening. The ideal diameter is 150–200 μm.

Complications

1. **Bleeding** occurs in about 50% of cases. It is usually slight and stops after several seconds. Persistent bleeding can be terminated by pressing the contact lens against the cornea.
2. **Iritis** is common and usually mild. Severe iritis, which may result in the formation of posterior synechiae (Fig. 9.146), is usually caused by over-treatment and inadequate post-laser steroid therapy.
3. **Corneal burns** may occur if a contact lens is not used or if the anterior chamber is shallow.
4. **Glare and diplopia** may rarely occur if the iridotomy is situated under the upper eyelid.

Fig. 9.146
Posterior synechiae following laser iridotomy (Courtesy of [illegible])

Diode laser cycloablation

This procedure lowers IOP by destroying part of the secretory ciliary epithelium, thereby reducing aqueous secretion. It is used mainly to control pain in intractable end-stage glaucoma, usually associated with permanent synechial angle closure.

1. **Technique**
   a. A peribulbar or sub-Tenon anaesthetic is administered.
   b. Laser settings are 1.5 seconds and 1500–2000 mW.
   c. The power is adjusted until a 'popping' sound is heard and then reduced to just below that level.
   d. Approximately 30 burns are placed 1.4 mm posteriorly to the limbus over 270°.
   e. A strong topical steroid is prescribed hourly on the day of treatment and then q.i.d. for 2 weeks.
2. **Complications.** Mild pain and anterior segment inflammation are common. Serious complications are rare and include chronic hypotony, scleral thinning, corneal decompensation and retinal or choroidal detachment. However, since the aim of the procedure is usually to relieve pain, vision-threatening complications do not have the same significance as those following conventional filtering procedures.
3. **Results.** The success rate is dependent on the type of glaucoma: frequently the procedure has to be repeated. Pain relief is generally good, but does not appear to be solely related to pressure control.

Trabeculectomy

Surgical techniques

Trabeculectomy

A trabeculectomy is a surgical procedure that lowers IOP by creating a fistula, which allows aqueous outflow from the anterior chamber to the sub-Tenon space. The fistula is protected or 'guarded' by a superficial scleral flap (Fig. 9.147).

1. The pupil must be miosed.
2. A flap of conjunctiva and Tenon capsule is fashioned. The flap may be limbal or fornix-based (Fig. 9.148).
3. Episcleral tissue is cleared. An outline of the proposed superficial scleral flap is made with wet-field cautery.
4. Incisions are made along the cautery marks through two-thirds of scleral thickness, to create a 'trapdoor' lamellar scleral flap (Fig. 9.149). This flap may be rectangular (3 × 4 mm) or triangular, according to preference.
5. The superficial flap is dissected forwards until clear cornea has been reached (Fig. 9.150).
6. A paracentesis is made in superotemporal peripheral clear cornea.
7. The anterior chamber is entered along the entire width of the trapdoor flap.

8. A block of deep sclera (1.5 × 2 mm) is excised with a knife and scissors (Figs 9.151 and 9.152) or a special punch (Fig. 9.153).
9. A peripheral iridectomy is performed (Fig. 9.154) in order to prevent blockage of the internal opening by the peripheral iris. Figure 9.155 shows the appearance from inside the eye.
10. The superficial scleral flap is sutured at its posterior corners so that it is lightly apposed to the underlying bed.
11. Alternatively, the flap may be sutured tightly with releasable sutures to reduce the risk of postoperative scleral flap leakage and shallow anterior chamber.
12. Balanced salt solution is injected into the anterior chamber through the paracentesis (Fig. 9.156a). This tests the patency of the fistula and facilitates the detection of any holes or leaks in the flap.

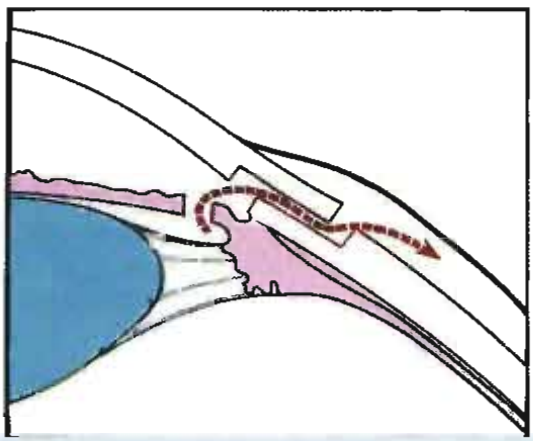

Fig. 9.147
Pathway of aqueous egress following trabeculectomy

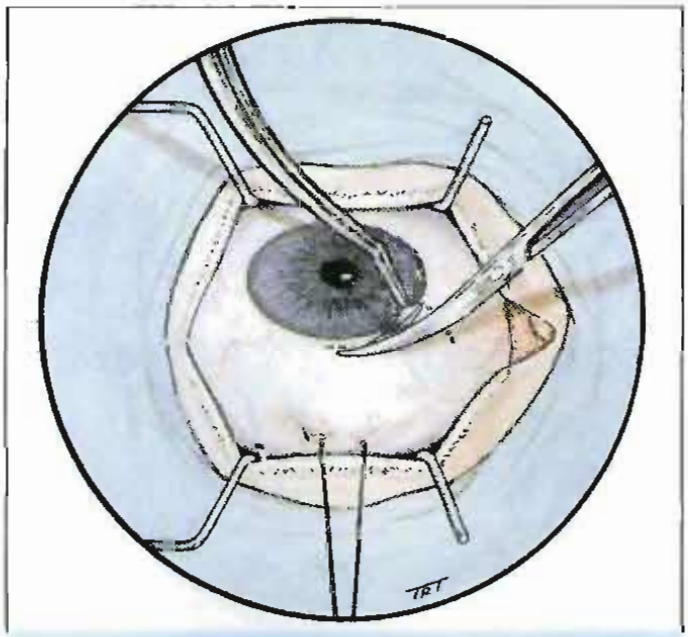

Fig. 9.148
Limbal conjunctival incision for a fornix-based flap

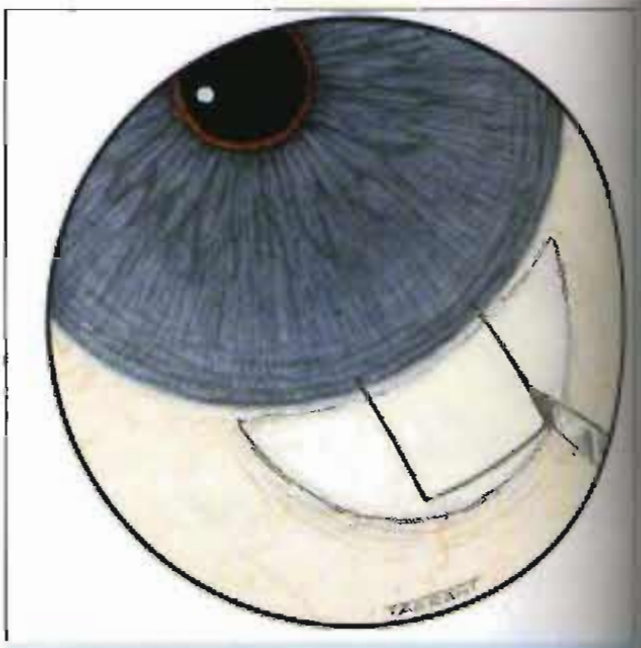

Fig. 9.149
Outline of the superficial scleral flap

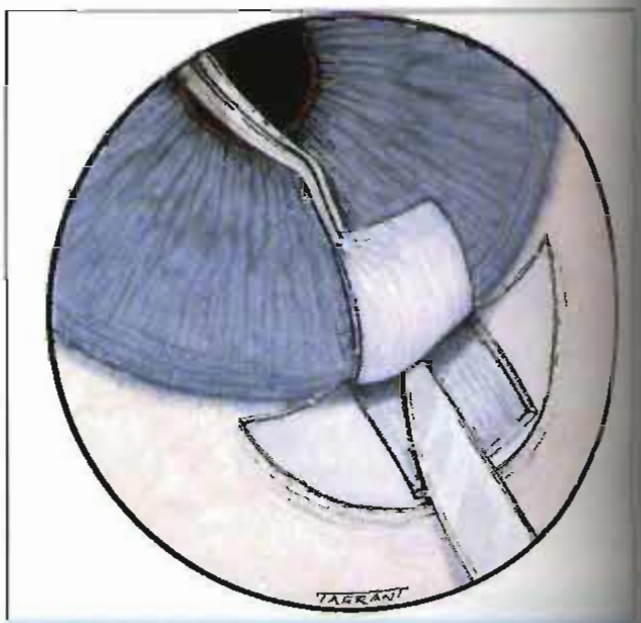

Fig. 9.150
Dissection of the superficial scleral flap

13. Conjunctiva/Tenon capsule flap is sutured (Fig. 9.156b). Irrigation through the paracentesis is repeated to produce a bleb, which is then checked for leakage.
14. A drop of atropine 1% is instilled.
15. A steroid and an antibiotic are injected under the inferior conjunctiva.

Combined trabeculectomy and phacoemulsification

Trabeculectomy and phacoemulsification can be performed using the same conjunctival and scleral incisions as follow

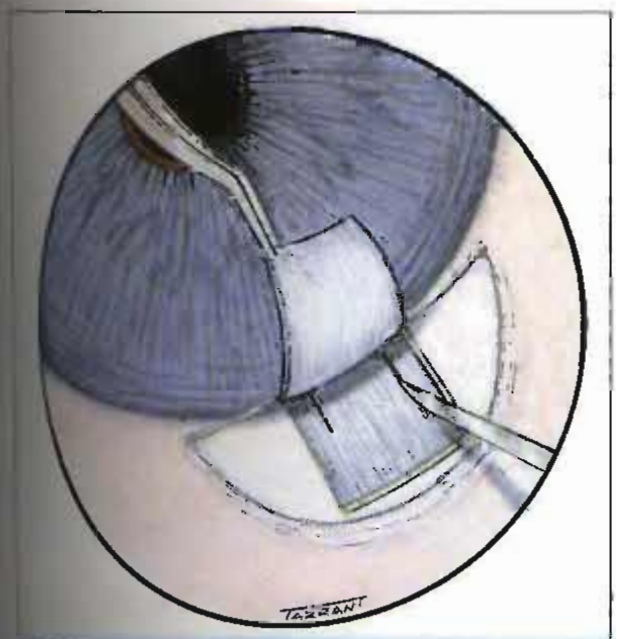

Fig. 9.151
Incisions for the deep sclerectomy

Fig. 9.153
Excision of the deep block with a punch

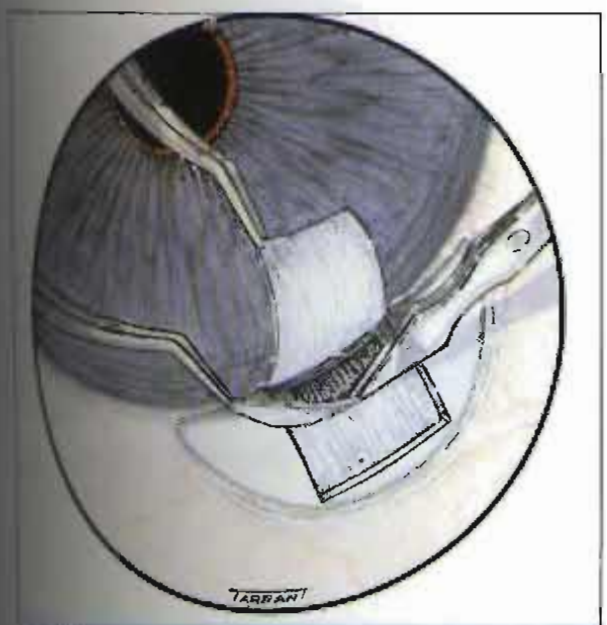

Fig. 9.152
Excision of the deep block with Vannas scissors

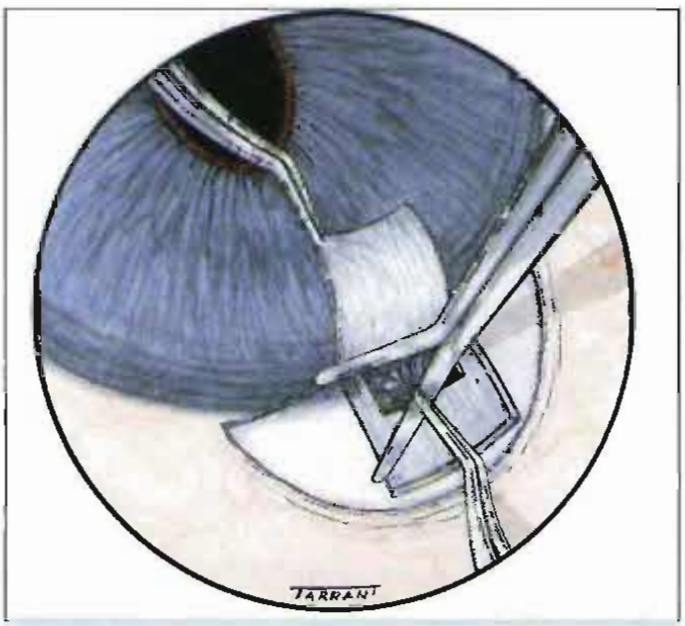

Fig. 9.154
Peripheral iridectomy

1. A conjunctival flap is fashioned.
2. A limbal scleral flap 3.5–4 mm wide, hinged at the limbus, is dissected.
3. A 'paracentesis' incision 2.8–3.2 mm wide is made into the anterior chamber.
4. Phacoemulsification is performed in the usual manner.
5. A foldable intraocular lens is inserted. If a rigid lens is used, the dimensions of the conjunctival and scleral flaps are adjusted accordingly from the outset.
6. The deep scleral block is removed.
7. A peripheral iridectomy is performed.
8. The scleral flap is closed.
9. The capsule and conjunctiva are sutured.

Postoperative complications

Shallow anterior chamber

This is one of the most common complications after trabeculectomy, and may be due to (a) *pupillary block*, (b) *overfiltration* or (c) *malignant glaucoma* (aqueous misdirection). Severe and sustained shallowing is uncommon, the chamber re-forming spontaneously in most cases. However, those that do not may develop severe complications such as peripheral anterior synechiae, corneal endothelial damage, cataract and hypotony-associated maculopathy.

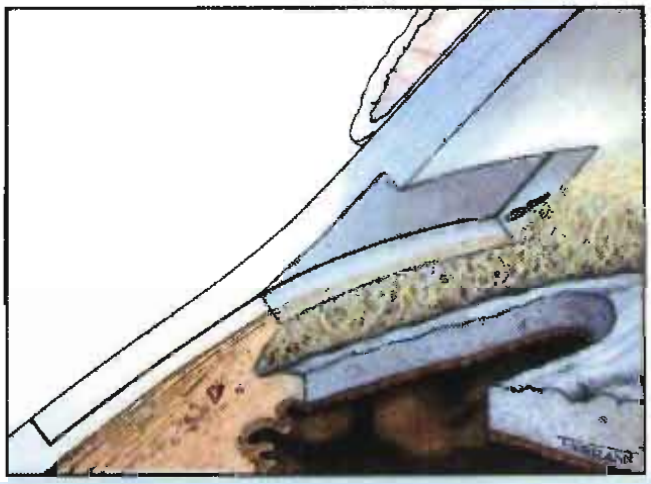

Fig. 9.155
Appearance following completed trabeculectomy

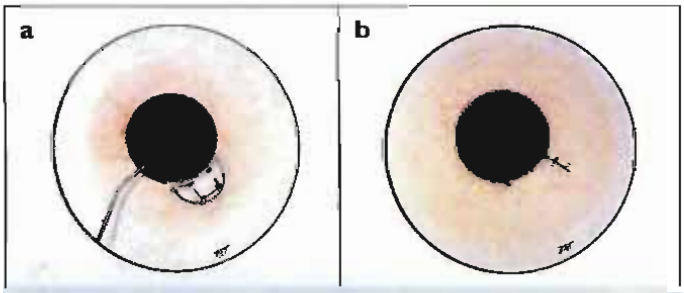

Fig. 9.156
(a) Injection of balanced salt solution into the anterior chamber; (b) sutured fornix-based flap

Evaluation

1. **Severity** of shallowing can be graded as follows:
   - Grade 1: peripheral iris apposition to the posterior corneal surface (Fig. 9.157).
   - Grade 2: pupillary border–corneal apposition (Fig. 9.158).
   - Grade 3: lens–corneal touch which, if unrelieved, may lead to endothelial decompensation (Fig. 9.159) and cataract formation (Fig. 9.160).
2. **The cause** is determined as follows:
   - The patency of the peripheral iridectomy is confirmed and the configuration of the iris studied to rule out pupillary block.
   - The filtration bleb is assessed.
   - A Seidel test is performed by instilling 2% fluorescein into the conjunctival sac or over the bleb. The bleb is then observed with a cobalt blue filter; if leaking, the fluorescein will become diluted by escaping aqueous (Fig. 9.161). Diluted fluorescein fluoresces bright green in contrast with 2% fluorescein (not as strongly).
   - The IOP is measured.
   - The fundus is examined for the presence of choroidal detachments (Fig. 9.162).

Pupillary block

1. **Cause** is a non-patent peripheral iridectomy.

Fig. 9.157
Shallow anterior chamber with peripheral iridocorneal apposition

Fig. 9.158
Very shallow anterior chamber with pupillary border-corneal apposition

Fig. 9.159
Lenticulo-corneal touch resulting in corneal oedema

2. **Signs**. High IOP, flat bleb, negative Seidel test and bombé with a non-patent iridectomy.
3. **Treatment**. Argon laser may be applied to the pigment epithelium at the iridectomy site if the anterior iris stroma

Fig 9.160
Anterior lens opacities following inappropriate management of a flat anterior chamber

Fig 9.161
Positive Seidel test

Fig 9.162
Choroidal detachment associated with hypotony

appears to have been largely penetrated, or a new laser iridotomy is performed.

Overfiltration

1. Causes

a. ***Scleral flap leakage*** due to insufficient resistance to outflow by the lamellar scleral flap. This can be prevented by initial tight closure of the flap with the option of subsequently increasing outflow in the early postoperative period by disrupting the sutures with an argon laser or releasing sutures that have been tied with slipknots. These manoeuvres are ineffective if undertaken later than 14 days postoperatively.

b. ***Bleb leakage*** through an inadvertent buttonhole or due to inadequate closure of the conjunctiva and Tenon capsule is perhaps the most common cause.

2. Signs.

- Low IOP.
- The bleb is well formed in a scleral flap leak and flat in a bleb leak.
- The Seidel test is negative in a scleral flap leak and positive in a bleb leak.
- The cornea may manifest signs of hypotony such as folds in Descemet membrane.
- Choroidal detachment may be present.

3. Treatment depends on the cause and degree of shallowing.

a. ***Initial*** conservative treatment in eyes without lenticulo-corneal touch.

- Topical atropine 1% to keep the pupil well dilated and prevent pupil block.
- Aqueous suppression with topical beta-blockers or oral acetazolamide may promote spontaneous healing by temporarily reducing aqueous flow through the fistula.
- Pinpoint bleb leaks may be sealed with cyanoacrylate or fibrin glue but sizeable conjunctival buttonholes or leaky incisions should be repaired surgically.
- In most cases this approach will be successful and the chamber will re-form within a few days.

b. ***Subsequent*** treatment if the aforementioned measures are ineffective involves temporary tamponade of the conjunctiva to enhance spontaneous healing by simple pressure patching, a large-diameter soft bandage contact lens, a collagen shield or a Simmons shell designed for the purpose. Such tamponade may result in deepening of the anterior chamber within a few hours, but if ineffective should be discontinued.

c. ***Definitive*** treatment for progressive shallowing and imminent or established lenticulo-corneal touch:

- The anterior chamber is re-formed with air, sodium hyaluronate or gas (SF_6).
- Choroidal detachment is drained only if very deep and in danger of touching (kissing choroidals).
- The scleral flap and conjunctiva are re-sutured. This may be difficult, since the tissue may now be friable.

Malignant glaucoma

Malignant (ciliary-block) glaucoma (aqueous misdirection 'syndrome') is rare but serious.

1. **Cause.** Blockage of aqueous flow at the pars plicata of the ciliary body, so that the aqueous is forced backwards into the vitreous.
2. **Signs.** A shallow anterior chamber in association with high IOP, absent bleb and negative Seidel test.
3. **Treatment**
   a. ***Initial conservative*** treatment.
      - Topical mydriatics (atropine 1% and phenylephrine 10%) to dilate the ciliary ring. This increases the distance between the ciliary processes and the equator of the lens, thereby tightening the zonule and pulling the lens posteriorly into its normal position.
      - Intravenous mannitol may be used if mydriatics are ineffective in order to shrink the vitreous gel and allow the lens to move posteriorly.
      - Aqueous suppressants are useful as adjuncts to control pressure.
   b. ***Subsequent*** treatment if medical therapy fails:
      - Nd:YAG laser may be fired through the iridectomy in order to disrupt the anterior hyaloid face and break the ciliary block. In pseudophakic eyes posterior capsulotomy and disruption of the anterior hyaloid face should be performed.
      - Pars plana vitrectomy is performed if laser therapy fails. Sufficient vitreous gel is excised to allow free flow of aqueous to the anterior chamber. If a vitreous cutter is not available the entrapped fluid may be aspirated with a 20-gauge needle inserted 3.5 mm posterior to the limbus and directed towards the centre of the globe.

Failure of filtration

Clinical evaluation

1. **Good filtration** is characterized by a low IOP and a bleb, which may take one of the following appearances:
   a. ***Type 1*** has a thin and polycystic appearance (Fig. 9.163) often with transconjunctival flow of aqueous.

Fig. 9.163
Thin polycystic filtration bleb

Fig. 9.164
Shallow diffuse filtration bleb

Fig. 9.165
Vascularized non-filtering bleb (Courtesy of J. Salmon)

   b. ***Type 2*** is shallow, thin-walled and diffuse, with a relatively avascular appearance in comparison with the surrounding conjunctiva (Fig. 9.164). Conjunctival epithelial microcysts are usually visible with high magnification.
2. **Poor filtration** is indicated by increasing IOP and a bleb with one of the following appearances:
   a. ***Type 3*** due to episcleral fibrosis, is flat, unassociated with microcystic spaces and manifests engorged surface blood vessels (Fig. 9.165).
   b. ***Type 4*** is an encapsulated bleb (Tenon cyst) which typically develops 2–8 weeks postoperatively. It is characterized by a localized, highly elevated, dome-shaped, firm, fluid-filled cavity of hypertrophied Tenon capsule with engorged surface blood vessels (Fig. 9.166). The cavity entraps aqueous humour and prevents filtration, although in some cases the IOP may not be elevated due to functional areas of filtration surrounding the bleb. Risk factors for encapsulated bleb formation include previous conjunctival surgery, laser trabeculoplasty, topical sympathomimetic therapy and an encapsulated bleb in the fellow eye.

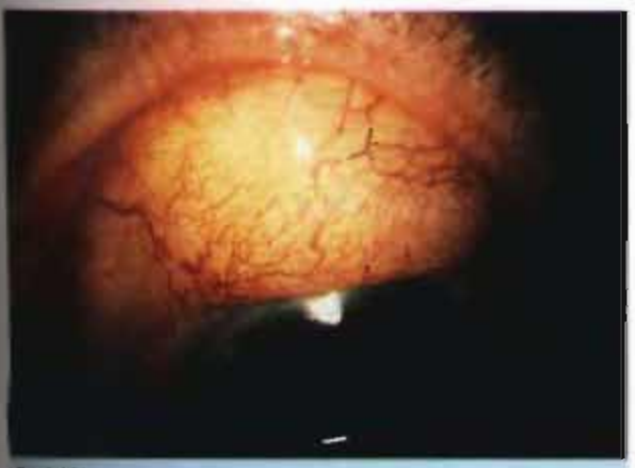

Fig. 9.166
Encapsulated non-filtering bleb

Causes of failure

Failure can be classified according to the site of blockage:

1. **Extraocular**
   - Subconjunctival and episcleral fibrosis is the most common cause of bleb failure; in many cases a well-formed bleb is never established. Intra- or postoperative subconjunctival haemorrhage may increase the risk of subsequent fibrosis.
   - Bleb encapsulation.
2. **Scleral**
   - Over-tight suturing of the scleral flap.
   - Gradual scarring in the scleral bed may lead to obstruction of the fistula at that level.
3. **Intraocular**
   - Blockage of the sclerostomy by vitreous, blood or uveal tissue.
   - Obstruction of the internal opening by a variety of thin membranes derived from surrounding cornea or sclera. This may be associated with poor surgical technique.

Management of failure

This is dependent on the actiology and may involve one or more of the following:

1. **Ocular compression** in an effort to force outflow through the surgical fistula is performed as follows:
   a. *Digital compression* is performed through the lower lid with the eyes closed and the patient looking straight ahead. Moderate digital pressure is applied for 5–10 seconds; the bleb is then examined. If the fistula is completely occluded the IOP and bleb appearance will be unchanged. If compression is effective, the IOP will have fallen and the bleb often appears inflated. The patient is instructed to carefully repeat this manoeuvre several times a day.
   b. *Focal compression* under topical anaesthesia is applied at the slit-lamp with a moistened sterile cotton bud at the edge of the scleral flap in an attempt to promote outflow.
2. **Suture manipulation** may be considered 7–14 days postoperatively if the eye has high IOP, a flat bleb and a deep anterior chamber.
   a. *Releasable sutures* can be cut or released according to the technique of initial placement.
   b. *Argon laser suture lysis* is useful if releasable sutures have not been used. It may be performed through a Hoskins (suture lysis lens) or a Zeiss four-mirror goniolens. The laser settings are 0.2 seconds duration, 50 μm spot size and 500–700 mW power.
3. **Needling** of an encysted bleb may be performed at the slit-lamp or operating microscope under topical anaesthesia. Balanced salt solution is injected subconjunctivally adjacent to the encapsulated bleb through a 27-gauge needle on a 1 ml syringe. The needle is then used to transfix and create a 2 mm incision in the fibrous wall of the cyst, taking care not to buttonhole the conjunctiva.
4. **Subconjunctival injection of 5-fluorouracil** may be used in the first 7–14 days to suppress episcleral fibrosis; 5 mg (0.1 ml of 50 mg/ml solution) is injected approximately 10 mm away from the bleb.
5. **Nd:YAG laser** may be useful in two settings:
   a. *Internal* gonioscopic reopening of a blocked internal ostium provided the tissue responsible can be identified gonioscopically and the eye already has a well-established bleb.
   b. *External* transconjunctival revision of a late-failing bleb due to episcleral fibrosis.
6. **Reoperation** to revise the existing trabeculectomy or perform a second filtering procedure in a different location. In these cases, adjunctive antimetabolite therapy may be appropriate to increase the chances of a successful outcome.
7. **Medical therapy** may need to be resumed if all else fails.

Late bleb leakage

1. **The cause** is dissolution of conjunctiva overlying the sclerostomy, following previous operative application of antimetabolites, particularly mitomycin C. Necrosis of the

Fig. 9.167
Severe chorioretinal folds in a hypotonous eye

Fig. 9.168
Avascular cystic bleb

Fig. 9.169
Appearance following repair of a leaking bleb

surface epithelium results in transconjunctival drainage of aqueous.

2. **Complications** of untreated leaks include corneal decompensation, peripheral anterior synechiae, suprachoroidal haemorrhage, chorioretinal folds (Fig. 9.167), hypotonous maculopathy and infection.
3. **Signs**
   - Low IOP and an avascular cystic bleb (Fig. 9.168).
   - Seidel testing is initially negative, and only multiple punctate staining areas (sweating) are seen. Later frank hole formation results in gross leakage with a positive test.
   - Shallow anterior chamber and choroidal detachment may be present in severe cases.
4. **Treatment** is difficult. The following are some of the methods used, none of which are universally successful.
   *a. **Initial*** treatment is as for early postoperative overfiltration but is seldom successful.
   *b. **Subsequent*** treatment depends on whether the leakage involves merely 'sweating' or is due to hole formation:
   - Sweating blebs may be treated by injection of autologous blood into the bleb, tissue glue or compressive sutures.
   - Full-thickness holes usually require revisional surgery such as conjunctival advancement to hood the existing bleb (Fig. 9.169), free conjunctival patch autografts with removal of the existing bleb and scleral grafts to limit flow through the sclerostomy.

Late onset bacterial infection

The thin-walled cystic bleb with a positive Seidel test, particularly if associated with a history of adjunctive antimetabolite therapy, is at significant risk because it drains transconjunctivally and is, therefore, most likely to provide a pathway for the entry of bacteria into the eye. All patients with such blebs should be warned of the possibility of late infection and strongly advised to report immediately should they develop a red and sticky eye, or blurred vision. Procedures that may traumatize the bleb such as fitting of contact lenses or gonioscopy should be avoided if possible. Other risk factors include full-thickness drainage procedures (e.g. Scheie thermosclerostomy), inferior location of the filtering bleb and inappropriate intermittent or prolonged use of topical antibiotics after the postoperative period.

'Blebitis'

In 'blebitis' the infection does not involve the vitreous.

1. **Presentation** is with mild symptoms such as discomfort and redness, which have usually been present for several days.
2. **Signs**
   - A whitened, milky bleb that appears to contain inflammatory material (Fig. 9.170).
   - Anterior uveitis may be absent (stage 1 blebitis) or present (stage 2 blebitis).
   - The red reflex is normal.
3. **Treatment** involves topical fluoroquinolones similar to that for bacterial keratitis (*see* Chapter 5). This is usually adequate but the patient should be watched carefully for evidence of vitreous involvement which may occasionally occur.

Fig. 9.170
'Blebitis' following trabeculectomy characterized by a white drainage bleb with surrounding conjunctival injection

Fig. 9.171
Endophthalmitis with hypopyon following trabeculectomy

Bleb-associated endophthalmitis

1. **Presentation** is with a short history of rapidly worsening vision, pain and redness.
2. **Signs**
   - White milky bleb.
   - Severe anterior uveitis which may be associated with hypopyon (Fig. 9.171).
   - Vitritis and impairment of the red reflex.
3. **Treatment** involves vitreous biopsy and intravitreal antibiotics (see Chapter 8).

NB: Successfully treated eyes remain at risk of recurrent infection.

Non-penetrating filtration surgery

In non-penetrating filtration surgery the anterior chamber is not entered, thus reducing the incidence of postoperative exfiltration and hypotony. In general, however, IOP reduction is inferior to that achieved by trabeculectomy; conventional filtration is therefore still the procedure of choice when the target IOP is in the lower teens. Non-penetrating surgery consists of fashioning two lamellar scleral flaps and excising the deep flap, leaving behind a thin membrane consisting of trabeculum/Descemet membrane through which aqueous diffuses from the anterior chamber to the subconjunctival space. The two currently used procedures are: (a) *deep sclerectomy*, in which bleb formation rarely occurs; and (b) *viscocanalostomy*, in which bleb formation is infrequent.

Deep sclerectomy

1. A fornix-based conjunctival flap is prepared.
2. A superficial partial-thickness scleral flap is dissected into clear cornea.
3. A second deeper partial-thickness scleral flap approximately 4 mm wide is dissected forward to the canal of Schlemm and is excised.
4. A collagen implant drainage device may be placed under the superficial scleral flap.
5. The superficial flap is loosely approximated and the conjunctival incision closed.

Viscocanalostomy

1. A fornix-based conjunctival flap is dissected.
2. A superficial partial-thickness flap is dissected to approximately one-third scleral thickness.
3. A second deeper scleral flap is dissected to provide access to Schlemm canal.
4. High-viscosity viscoelastic substance is injected into Schlemm canal with a special cannula.
5. A Descemet 'window' is created by gently dissecting the deep flap anterior to Schlemm canal and then excising it.
6. The superficial scleral flap is tightly sutured to minimize subconjunctival fluid flow and bleb formation.
7. Viscoelastic substance is injected into the area of the sclerotomy.
8. The conjunctiva is closed.

Adjunctive antimetabolites

Adjunctive antimetabolites inhibit the natural healing response that may preclude successful filtration surgery. They should, however, be used with caution because of the serious nature of potential complications, and primarily considered in the context of known risk factors for failure of trabeculectomy.

Indications

1. **High risk factors**
   - Neovascular glaucoma.
   - Previous failed trabeculectomy or artificial filtering devices.
   - Certain secondary glaucomas (e.g. inflammatory, post-traumatic angle recession and iridocorneal endothelial syndrome).
   - Chronic cicatrizing conjunctival inflammation.
2. **Intermediate risk factors**
   - Patients on topical antiglaucoma medication (particularly sympathomimetics) for over 3 years.
   - Previous conjunctival surgery.
   - Combined procedure for glaucoma and cataract.
3. **Low risk factors**
   - Black patients.
   - Patients under the age of 40 years.

NB: In uncomplicated glaucoma the use of low-dose antimetabolites may improve long-term control of IOP but this benefit should be weighed against possible complications such as corneal epithelial defects, chronic hypotony and late-onset bleb leakage.

General precautions

- Antimetabolite therapy should be used with great caution when the conjunctiva has been recessed or where the limbal stem cell population is decreased (e.g. alkali burns, ocular pemphigoid).
- The filtration site should never be placed inferiorly because of the increased risk of late intraocular infection.
- The antimetabolite must not come into contact with the edges of the conjunctival incisions or the corneal endothelium.
- Tenon capsule and conjunctiva should be sutured separately in two layers, with a round-bodied needle.
- Patients should be advised of the potential late complications, in particular the high incidence of cystic bleb formation. They should also be made aware that additional surgery may be required in the event of late hypotony. Because of the potential for late bleb-related endophthalmitis they should be told of the risks associated with contact lens wear, swimming in a public pool and the danger of using contaminated drops.

5-Fluorouracil

5-Fluorouracil (5-FU) inhibits DNA synthesis and is active on the 'S' phase (synthesis phase) of the cell cycle. Fibroblastic proliferation is inhibited, but fibroblastic attachment and migration are unaffected. The technique is as follows:

1. A conjunctival flap is dissected.
2. A cellulose sponge measuring 4.5 × 4.5 mm is soaked in a 50 mg/ml solution of 5-FU.
3. The sponge is placed under the dissected flap of Tenon capsule at the site of filtration, making sure that the edges of the conjunctival incision are not exposed to the drug.
4. The sponge is removed after 5 minutes.
5. The space between the conjunctiva and episclera is thoroughly irrigated with balanced salt solution.
6. The trabeculectomy is completed.

Mitomycin C

Mitomycin C (MMC) is an alkylating agent rather than an antimetabolite which selectively inhibits DNA replication, mitosis and protein synthesis. The drug inhibits proliferation of fibroblasts, suppresses vascular ingrowth and *in vitro* has been shown to be much more potent than 5-FU. Optimum concentration and exposure time are not known and vary between 0.2–0.5 mg/ml and 1–5 minutes. In general, low or intermediate risk indicates use of a low concentration (0.2 mg/ml), while high risk implies the need for a higher concentration (0.4–0.5 mg/ml). Higher concentrations and extended exposure times are associated with an increased risk of complications. The technique of application is the same as for 5-FU and great care should be taken to prevent contamination of the anterior chamber.

Artificial drainage shunts

Artificial drainage shunts are plastic devices which create a communication between the anterior chamber and sub-Tenon space. All such shunts consist of a tube attached to a posterior episcleral explant. Some contain pressure-sensitive valves for regulation of aqueous flow. Because of the many postoperative complications associated with this type of surgery, drainage shunts should be installed only by surgeons thoroughly trained in their use.

Indications

- Uncontrolled glaucoma despite previous trabeculectomy with adjunctive antimetabolite therapy.
- Secondary glaucoma where routine trabeculectomy with or without adjunctive antimetabolites, is unlikely to be successful. *Examples include neovascular glaucoma*, aniridia and glaucoma following traumatic anterior segment disruption.
- Severe conjunctival scarring precluding accurate dissection of the conjunctiva.
- Certain congenital glaucomas where conventional procedures have failed (i.e. goniotomy, trabeculotomy and trabeculectomy).

Implant types

The currently used implants are the Molteno (Fig. 9.172), Baerveldt, Krupin and Ahmed. They are based on a design

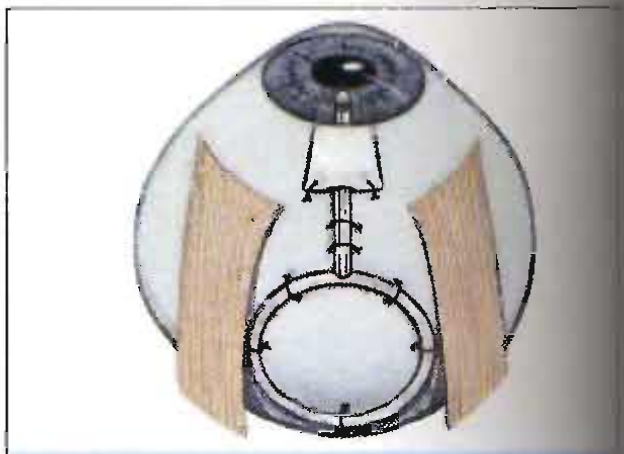

Fig. 9.172
Molteno implant

inally described by Molteno, which incorporates a scleral implant to promote the formation of a functioning bleb. An open tube, one end of which is placed in the anterior chamber, drains aqueous humour into an encapsulated area around the implant located 10–12 mm posterior to the limbus. Reduction of IOP is due to passive, pressure-dependent flow of aqueous across the capsular wall. The magnitude of pressure reduction depends on the resistance to aqueous flow (the thicker the capsule, the higher the IOP) and the total surface area of encapsulation (the larger the surface, the lower the IOP).

Complications

1. **Excessive drainage** may occur due to leakage around or down the tube and result in a shallow anterior chamber (Fig. 9.173). Leakage down the tube may be minimized by the use of releasable or dissolvable sutures to occlude the tube during the early postoperative period.
2. **Corneal decompensation** secondary to endothelial touch by a poorly positioned tube.
3. **Cataract** may develop if the end of the tube touches the lens.
4. **Tube retraction** from the anterior chamber is uncommon, but may occur if the tube has been cut too short.
5. **Tube erosion** through the conjunctiva (Fig. 9.174) can be avoided by placing a donor scleral flap between the tube and Tenon capsule.
6. **Drainage failure** may occur as a result of blockage of the end of the tube by vitreous, blood or iris tissue.
7. **Diplopia** due to muscle imbalance has been reported, particularly if the footplate passes under a muscle or if a device with a large drainage area has been used.
8. **Bleb encapsulation** over the footplate (Fig. 9.175) may result in poor drainage. This occurs in about 10% of cases and is the most significant late complication.
9. **Late endophthalmitis.**

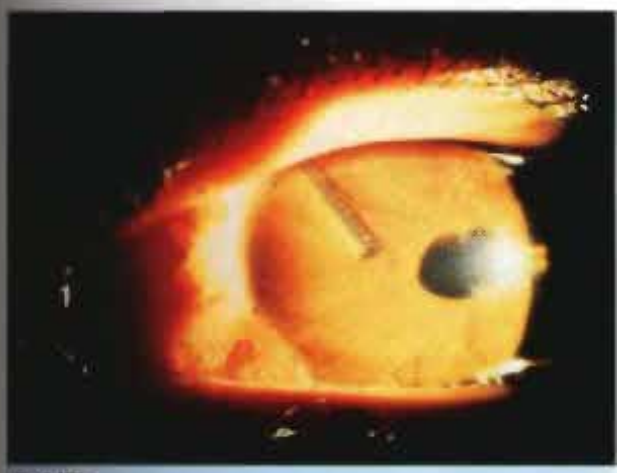

Fig. 9.173
Flat anterior chamber secondary to excessive drainage by an artificial shunt (Courtesy of J. Salmon)

Fig. 9.174
Erosion of a drainage tube through the conjunctiva (Courtesy of J. Salmon)

Fig. 9.175
Encapsulation of the bleb over the footplate (Courtesy of J. Salmon)

Results

These depend on the type of glaucoma. An IOP < 21 mmHg is achieved in 50–70% of cases but topical medication is often required to maintain the IOP at this level. Less than 33% of cases achieve adequate control of IOP without additional medical therapy. The long-term success rate in neovascular glaucoma is particularly disappointing because of progressive retinal disease with loss of vision and late development of phthisis bulbi. Adjunctive mitomycin C may enhance the success rate of drainage shunt surgery.

CHAPTER 10

Uveitis

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Introduction

Classification

Uveitis, by strict definition, is an inflammation of the uveal tract. However, the term is now used to describe many forms of intraocular inflammation involving not only the uvea, but also adjacent structures. Uveitis may be classified on the basis of (a) *anatomy*, (b) *clinical features* and (c) *aetiology*.

Anatomical classification (Fig. 10.1)

1. **Anterior uveitis** may be subdivided into:
   a. *Iritis*, in which inflammation predominantly affects the iris.
   b. *Iridocyclitis*, in which both the iris and the anterior part of the ciliary body (pars plicata) are equally involved.
2. **Intermediate uveitis** is characterized by involvement predominantly of the posterior part of the ciliary body (pars plana), the extreme periphery of the retina and the underlying choroid.
3. **Posterior uveitis** involves inflammation of the choroid and retina posterior to the vitreous base.
4. **Panuveitis** implies involvement of the entire uveal tract.

> **NB:** Anterior uveitis is the most common type, followed by intermediate, posterior and panuveitis.

Clinical classification

According to the mode of onset and duration, uveitis may be acute or chronic.

1. **Acute uveitis** usually has a sudden, symptomatic onset and persists for up to 3 months. If the inflammation recurs following the initial attack, it is referred to as recurrent acute.
2. **Chronic uveitis** persists for longer than 3 months. The onset is frequently insidious and may be asymptomatic, although acute or subacute exacerbations may occur.

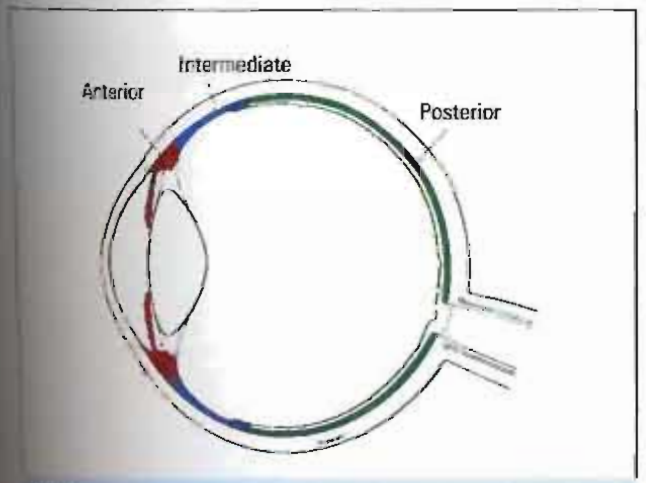


Fig. 10.1
Anatomical classification of uveitis

Aetiological classification

Exogenous uveitis is caused by external injury to the uvea or invasion by micro-organisms (or other agents) from without. Endogenous uveitis is caused by micro-organisms (or other agents) from within the patient. The following are the main types:

1. **Associated with a systemic disease** (e.g. sarcoidosis).
2. **Infections** with bacteria (e.g. tuberculosis), fungi (e.g. candidiasis) and viruses (e.g. herpes zoster).
3. **Infestations** with protozoa (e.g. toxoplasmosis) or nematodes (e.g. toxocariasis).
4. **Idiopathic specific uveitis entities** are a group of unrelated disorders unassociated with underlying systemic disease but with special characteristics of their own warranting independent description (e.g. Fuchs uveitis syndrome).
5. **Idiopathic non-specific uveitis entities** which do not fall into any of the above categories consititute about 25% of cases.

Clinical features

Anterior uveitis

Symptoms

1. **Acute anterior uveitis** is characterized by photophobia, pain, redness, decreased vision and lacrimation.
2. **Chronic anterior uveitis** may be asymptomatic or give rise to mild redness and the perception of floaters.

Signs

1. **Circumcorneal (ciliary) injection** in acute anterior uveitis has a violaceous hue (Fig. 10.2).
2. **Keratic precipitates** (KP) are cellular deposits on the corneal endothelium. Their characteristics and distribution may indicate the probable type of uveitis. KP most

Fig. 10.2
Ciliary injection in acute anterior uveitis

commonly form in the mid and inferior zones of the cornea, due to convection currents in the anterior chamber. However, in Fuchs uveitis syndrome, they are scattered throughout the endothelium.

a. ***Endothelial dusting*** by myriads of cells occurs in acute anterior uveitis, as well as during subacute exacerbations of chronic inflammation (Fig. 10.3).

b. ***Medium-size*** KP occur in most types of acute and chronic anterior uveitis (Fig. 10.4).

c. ***Large*** KP are usually of the 'mutton fat' variety, with a greasy, waxy appearance, typically occurring in granulomatous uveitis (Fig. 10.5).

d. ***Old*** KP are pigmented (Fig. 10.6) and, if large, may develop a 'ground-glass' (hyalinized) appearance (Fig. 10.7).

3. Cells are indicative of active inflammation.

a. ***Aqueous cells*** are graded according to the number observed in an oblique slit beam, 3 mm long and 1 mm wide, with maximal light intensity and magnification.

- <5 cells = +/–
- 5–10 cells = +1
- 11–20 cells = +2
- 21–50 cells = +3
- >50 cells = +4
- hypopyon (Fig. 10.8)

Fig. 10.5
Mutton fat keratic precipitates

Fig. 10.3
Endothelial dusting in acute anterior uveitis

Fig. 10.6
Old pigmented keratic precipitates

Fig. 10.4
Medium-size keratic precipitates

Fig. 10.7
Old 'ground-glass' keratic precipitates

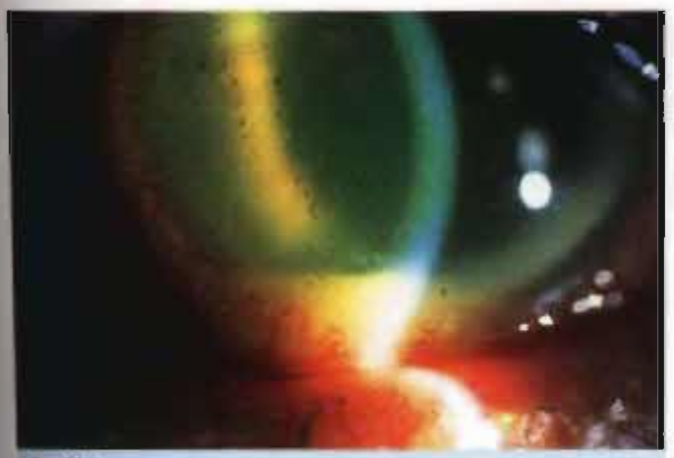


Fig. 10.8
Hypopyon in acute anterior uveitis

Fig. 10.11
Koeppe nodules in granulomatous anterior uveitis

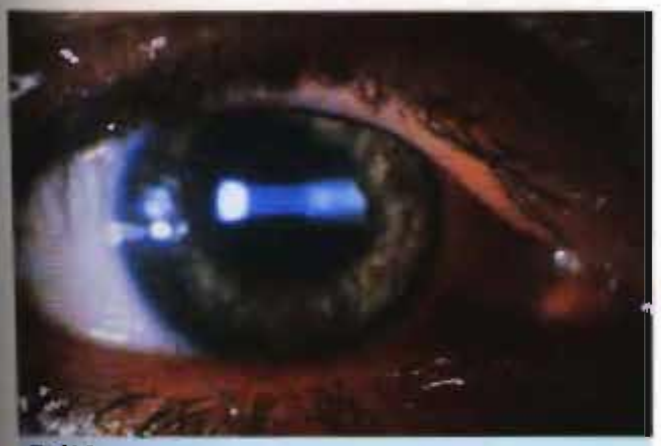


Fig. 10.9
Dense aqueous flare

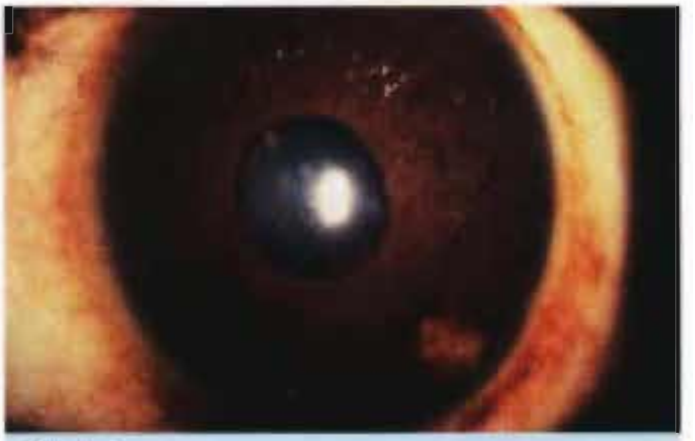


Fig. 10.12
Busacca nodule in granulomatous anterior uveitis

Fig. 10.10
Fibrinous exudate in severe acute anterior uveitis

b. ***Anterior vitreous cells*** should be compared in number with those in the aqueous. In iritis, aqueous cells far exceed the number of vitreous cells.

4. **Aqueous flare** is due to scattering of light (Tyndall effect) by proteins that have leaked into the aqueous humour through damaged iris blood vessels (Fig. 10.9). In the absence of cells, aqueous flare is not indicative of active inflammation and does not merit treatment. It is graded using the same setting on the slit-lamp as for cells.
   - faint: just detectable = +1
   - moderate: iris details clear = +2
   - marked: iris details hazy = +3
   - intense with fibrinous exudate = +4 (Fig. 10.10).
5. **Iris nodules** are a feature of granulomatous inflammation.
   a. *Koeppe* nodules are small and situated at the pupillary border (Fig. 10.11).
   b. *Busacca* nodules are less common and located away from the pupil (Fig. 10.12).

Complications

1. **Posterior synechiae** are adhesions between the iris and anterior lens capsule, which may form with ease during an attack of acute anterior uveitis and also in eyes with

moderate-to-severe chronic anterior uveitis (Fig. 10.13). Posterior synechiae extending for 360° around the pupillary border (seclusio pupillae) prevent the passage of aqueous humour from the posterior to the anterior chamber, giving rise to a forward bowing of the peripheral iris (iris bombé) (Fig. 10.14). This may lead to closure of the angle of the anterior chamber by the peripheral iris, with secondary elevation of intraocular pressure (see Chapter 9). After the posterior synechiae have been broken down, an imprint of iris pigment may remain on the anterior lens capsule (Fig. 10.15).

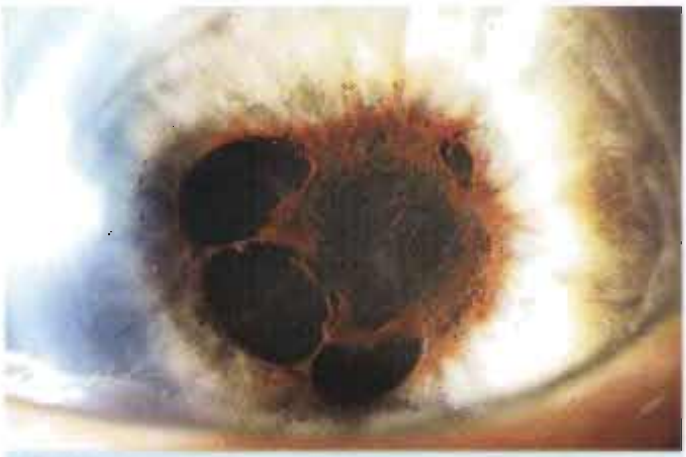


Fig. 10.13
Posterior synechiae

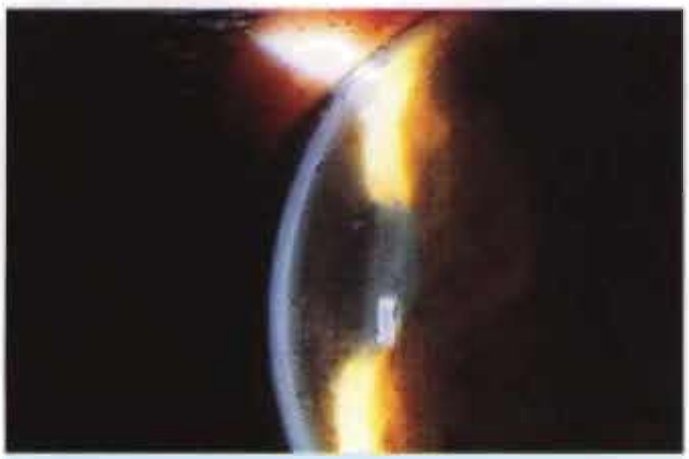


Fig. 10.14
Iris bombé

2. **Other complications** of chronic or recurrent anterior uveitis include band keratopathy, cataract, glaucoma, macular oedema, cyclitic membrane formation and phthisis bulbi.

Intermediate uveitis

1. **Symptoms** are initially floaters and later impairment of visual acuity due to cystoid macular oedema.
2. **Signs**. Cellular infiltration of the vitreous (vitritis) with fewer cells in the anterior chamber. Absence of focal inflammatory lesions in the posterior fundus.
3. **Complications** include cystoid macular oedema, cyclitic membrane formation, cataract and tractional retinal detachment.

Intermediate uveitis is discussed in more detail later.

Posterior uveitis

Symptoms

These are floaters and impaired vision. A patient with a peripheral inflammatory lesion will complain of floaters and may have only minimal blurring of vision. On the other hand, active choroiditis involving the fovea or papillomacular bundle will primarily cause loss of central vision, and the patient may not notice vitreous opacities.

Signs

1. **Vitreous** signs include cells, flare, opacities (Fig. 10.16) and posterior vitreous detachment. The posterior hyaloid face may be covered by inflammatory precipitates comparable to KP.

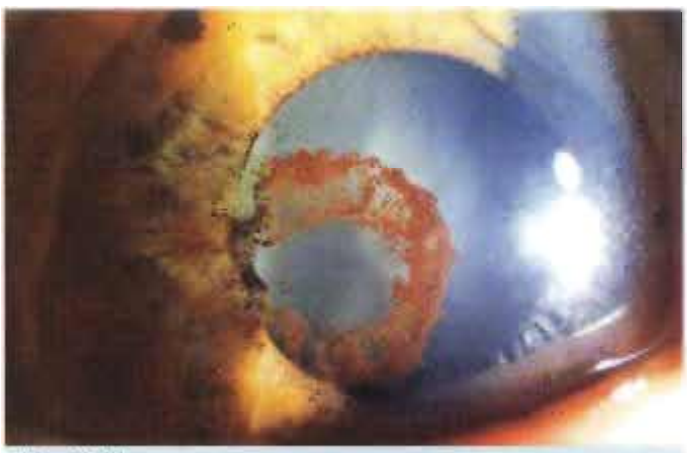


Fig. 10.15
Residual pigment following breakdown of posterior synechiae

Fig. 10.16
Coarse vitreous opacities in posterior uveitis

2. **Choroiditis** is characterized by deep, yellow or greyish patches with fairly well-demarcated borders (Fig. 10.17). Inactive lesions appear as white, well-defined areas of chorioretinal atrophy with pigmented borders (Fig. 10.18).

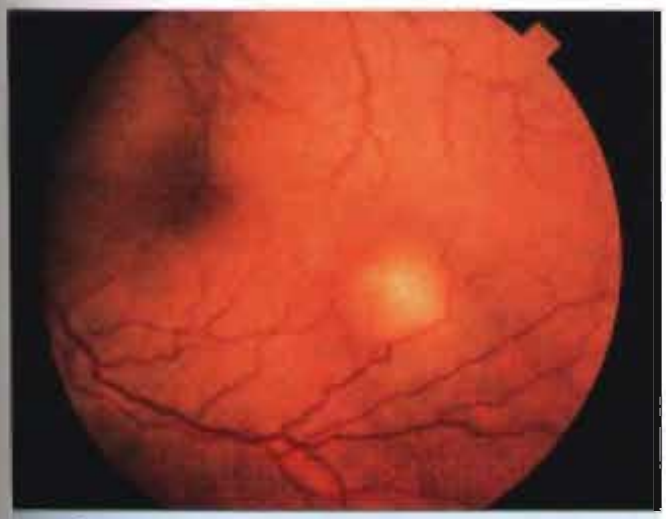


Fig. 10.17
Active focal choroiditis

Fig. 10.18
Old multifocal choroiditis

3. **Retinitis** gives the retina a white cloudy appearance, with obscuration of retinal vessels (Fig. 10.19). The outline of the inflammatory focus is indistinct, rendering exact demarcation between healthy and affected retina difficult.
4. **Vasculitis** most frequently involves retinal veins (periphlebitis) and less commonly arteries (periarteritis). Active periphlebitis is characterized by a fluffy white haziness surrounding the blood column (Fig. 10.20). Involvement is patchy, with irregular extensions outside the vessel wall. Perivascular accumulation of granulomatous tissue in severe periphlebitis may give rise to 'candlewax drippings' (*see* Fig. 10.29).
5. **'Spill-over' anterior uveitis** is common.

Fig. 10.19
Active focal retinitis

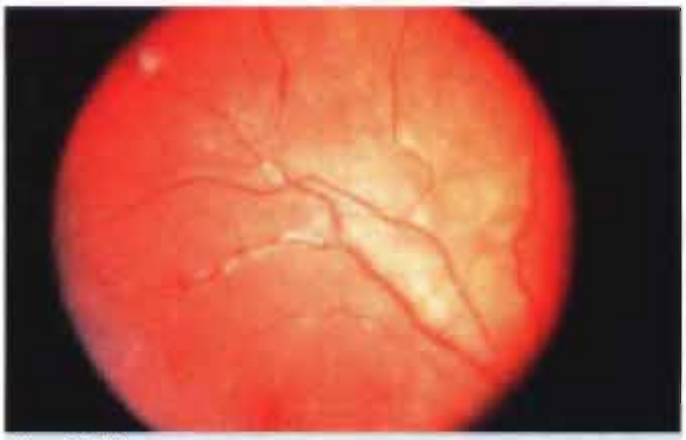


Fig. 10.20
Active periphlebitis

Complications

These include direct involvement of the macula by the inflammatory process, cystoid macular oedema, macular ischaemia, epiretinal membrane formation, vascular occlusions, choroidal neovascularization, retinal detachment and consecutive optic neuropathy.

Morphological classification

1. **Focal** in which there is a solitary inflammatory focus (e.g. toxoplasmosis).
2. **Multifocal** in which there are several separate foci (e.g. birdshot retinochoroidopathy).
3. **Geographical** in which there is a large confluent area of inflammation (e.g. cytomegalovirus retinitis).

Treatment

The main aims of treating uveitis are to prevent vision-threatening complications, to relieve discomfort and to treat the underlying disease, if possible. The three groups of drugs in current use are (a) *mydriatics*, (b) *steroids* and (c) *systemic immunosuppressive agents*. Uveitis of infective aetiology should be treated with the appropriate antimicrobial or antiviral agent.

Mydriatics

Preparations

1. **Short-acting:**
   - Tropicamide (0.5% and 1%) has a duration of 6 hours.
   - Cyclopentolate (0.5% and 1%) has a duration of 24 hours.
   - Phenylephrine (2.5% and 10%) has a duration of 3 hours but no cycloplegic effects.
2. **Long-acting:** atropine 1% is the most powerful cycloplegic and mydriatic with a duration of action lasting up to 2 weeks.

Indications

1. **To promote comfort** by relieving spasm of the ciliary muscle and pupillary sphincter, usually with atropine, although it is usually unnecessary to use this agent for more than 1–2 weeks. Once the inflammation shows signs of subsiding it can be substituted by a short-acting mydriatic, such as tropicamide or cyclopentolate.
2. **To prevent formation of posterior synechiae** by using a short-acting mydriatic which keeps the pupil mobile. In mild cases of chronic anterior uveitis the mydriatic can be instilled once at bedtime to prevent difficulties with accommodation during the day. Moreover the pupil should not be kept constantly dilated because posterior synechiae can still form in the dilated position. In young children, constant uniocular atropinization may induce amblyopia.
3. **To break down recently formed synechiae** with intensive topical mydriatics (atropine, phenylephrine) or subconjunctival injections of Mydricaine (adrenaline, atropine and procaine).

Steroids

Steroids are the mainstay of treatment. They can be administered (a) *topically* as drops or ointment, (b) by *periocular injection*, (c) by *intravitreal injection* or (d) *systemically*. Steroids, by whatever route, should be generally commenced at a high dose, which is subsequently tapered, once the inflammation comes under control.

Topical administration

Topical steroids are useful only for anterior uveitis because they do not reach therapeutic levels behind the lens. Strong steroids such as dexamethasone, betamethasone and prednisolone are preferable to weaker preparations such as fluorometholone. A solution penetrates the cornea better than a suspension or ointment. Ointment can, however, be instilled at bedtime. The frequency of instillation of drops depends on the severity of inflammation and can vary from one drop every 5 minutes to a drop every other day.

1. **Treatment of acute anterior uveitis** is relatively straightforward and depends on the severity of inflammation. Administration is initially very frequent (e.g. every 15 minutes) for a few hours and then gradually tapered to q.i.d. after several days. Once the inflammation is well controlled the frequency can be further reduced by one drop/week and often discontinued altogether by 5–6 weeks. Tissue plasminogen activator (12.5 μg in 0.1 ml) injected into the anterior chamber (intracamerally) with a 25-gauge needle may dissolve fibrinous exudate and prevent subsequent pupil block glaucoma.
2. **Treatment of chronic anterior uveitis** is more difficult because the inflammation may last for months and even years. Acute exacerbations with +4 aqueous cells are initially treated in the same way as acute anterior uveitis. If the inflammation is controlled with no more than +1 aqueous cells, the rate of instillation can be gradually further reduced by one drop/month and then sometimes discontinued.

> ***NB:*** Following cessation of treatment, the patient should be re-examined within a few days to ensure that the uveitis has not recurred.

3. **Complications**
   - *a. Glaucoma* in susceptible individuals (*see* Chapter 9).
   - *b. Cataract* can be induced by both systemic and, less frequently, topical steroid administration. The risk increases with dose and duration of therapy.
   - *c. Corneal* complications, which are uncommon, include secondary infection with bacteria and fungi, recrudescences of herpes simplex keratitis, and corneal melting, which may be enhanced by inhibition of collagen synthesis.
   - *d. Systemic* side effects may occasionally occur following prolonged administration, particularly in children.

Periocular injections

1. **Advantages over topical administration**
   - Therapeutic concentrations behind the lens may be achieved.
   - Water-soluble drugs, incapable of penetrating the cornea when given topically, can enter the eye transsclerally, when given by periocular injection.
   - A long-lasting effect can be achieved with depot preparations such as triamcinolone acetonide (Kenalog) or methylprednisolone acetate (Depomedrone).

2. Indications
- Severe acute anterior uveitis, especially in patients with ankylosing spondylitis with a marked fibrinous exudate in the anterior chamber or hypopyon (*see* Figure 10.8).
- As an adjunct to topical or systemic therapy in resistant chronic anterior uveitis.
- Intermediate uveitis.
- Poor patient compliance with topical or systemic medication.
- At the time of surgery in eyes with uveitis.

3. Conjunctival anaesthesia

a. A topical anaesthetic such as amethocaine is instilled at 1-minute intervals for 5 minutes.

b. A small cotton pledget impregnated with amethocaine (or equivalent) is placed into the conjunctival sac at the site of injection and left there for 5 minutes.

4. Anterior sub-Tenon Injection

a. 1 ml of steroid is drawn up into a 2 ml syringe and the drawing-up needle replaced with a 25-gauge 3/8 inch (10 mm) needle.

b. The patient is asked to look away from the site of injection: most frequently up.

c. With non-toothed forceps, the conjunctiva and Tenon capsule are grasped and lifted.

d. With the bevel away from the globe, the needle is passed through the conjunctiva and Tenon capsule at the point where they are grasped.

e. 0.5 ml of steroid is injected slowly.

5. Posterior sub-Tenon injection

a. 1.5 ml steroid is drawn up into a 2 ml syringe and the drawing-up needle replaced with a 25-gauge 5/8-inch (16 mm) needle.

Fig. 10.21
Posterior sub-Tenon steroid injection (Courtesy of V. Tanner)

b. The patient is asked to look away from the site of injection: most frequently inferonasally when the injection is being given superotemporally.

c. The bulbar conjunctiva is penetrated with the tip of the needle, bevel towards the globe, slightly on the global side of the fornix (Fig. 10.21).

d. The needle is slowly inserted posteriorly, following the contour of the globe, keeping it as close to the globe as possible. In order not to penetrate the globe accidentally, wide side-to-side motions are made as the needle is being inserted and the limbus watched; movement of the limbus means that the sclera has been engaged!

e. When the needle has been advanced to the hub and cannot be inserted any further, the plunger is slightly withdrawn and, if no blood has entered the syringe, 1 ml injected. If the needle is too far away from the globe, adequate trans-scleral absorption of steroid will not occur.

NB: An alternative method is to incise the conjunctiva and Tenon's capsule, and to perform the injection with a blunt sub-Tenon or lacrimal cannula.

Intravitreal injection

Intravitreal steroid injection of triamcinolone acetonide (2 mg in 0.05 ml) is currently under evaluation. It has been used successfully in resistant uveitic chronic cystoid macular oedema.

Systemic therapy

1. Preparations

a. Oral prednisolone 5 mg is the main preparation. Enteric coated tablets are useful in patients with acid-peptic disease.

b. Injections of adrenocorticotrophic hormone (ACTH) are useful in patients intolerant to oral steroids.

2. Indications
- Intractable anterior uveitis resistant to topical therapy and anterior sub-Tenon injections.
- Intermediate uveitis unresponsive to posterior sub-Tenon injections.
- Certain types of posterior or panuveitis, particularly with severe bilateral involvement.

3. General rules of administration
- Start with a large dose and then reduce.
- A reasonable starting dose of prednisolone is 1 mg/kg per day given in a single morning dose.
- Once the inflammation is brought under control, reduce the dose gradually over several weeks.
- If steroids are given for less than 2 weeks there is no need for gradual reduction.

4. Side effects depend on the duration of administration.

a. Short-term therapy may cause dyspepsia, mental changes, electrolyte imbalance, aseptic necrosis of the head of the femur and, very rarely, hyperosmolar hyperglycaemic non-ketotic coma.

b. Long-term therapy may cause a Cushingoid state (*see* Chapter 20), osteoporosis, limitation of growth in children, reactivation of infections such as TB, cataract and increase in severity of pre-existing conditions such as diabetes and myopathy.

Immunosuppressive agents

Immunosuppressive agents used in the treatment of uveitis are (a) *antimetabolites* (cytotoxics) and (b) *T-cell inhibitors*.

Indications

1. **Sight-threatening uveitis**, which is usually bilateral, non-infectious, reversible and has failed to respond to *adequate* steroid therapy.
2. **Steroid-sparing therapy** in patients with intolerable side effects from systemic steroids. Once a patient has been started on an immunosuppressive drug and the appropriate dose ascertained, treatment should continue for 6–24 months, after which gradual tapering and discontinuation of medication should be attempted over the next 3–12 months. However some patients may require long-term therapy for control of disease activity.

Antimetabolites

1. **Azathioprine**
   - *a. Indications*: mainly Behçet disease.
   - *b. Dose* is 1–3 mg/kg per day (50 mg tablet) administered orally once daily or in divided doses.
   - *c. Side effects* include bone marrow suppression, gastrointestinal disturbance and hepatotoxicity.
   - *d. Monitoring* involves a complete blood count every 4–6 weeks and liver function tests every 12 weeks.
2. **Methotrexate**
   - *a. Indications* include a variety of chronic non-infectious uveitides unresponsive to conventional steroid therapy.
   - *b. Dose* is 7.5–25 mg in a single dose once weekly.
   - *c. Side effects*: bone marrow suppression, hepatotoxicity and pneumonitis are serious but rarely occur with low-dose administration. The most common side effects are gastrointestinal.
   - *d. Monitoring* involves full blood counts and liver function tests every 1–2 months.
3. **Mycophenolate mofetil**
   - *a. Indications* are as yet not established but it may prove a useful alternative to other antimetabolites.
   - *b. Dose* is 1 g b.d.
   - *c. Side effects* include gastrointestinal disturbance and bone marrow suppression.
   - *d. Monitoring* involves a full blood count initially weekly for 4 weeks and then less frequently.

T-cell inhibitors

1. **Cyclosporin**
   - *a. Indications* include Behçet disease, intermediate uveitis, Vogt Koyanagi–Harada syndrome, birdshot retinochoroidopathy, sympathetic ophthalmitis and retinal vasculitis.
   - *b. Dose* is usually 2–5 mg/kg per day in two divided doses.
   - *c. Side effects* include hypertension, nephrotoxicity, hirsutism, hepatotoxicity and gingival hyperplasia.
   - *d. Monitoring* involves blood pressure, full blood count, renal and liver function tests every 6 weeks.
2. **Tacrolimus (FK 506)**
   - *a. Indications* are not yet established. Currently the drug is being used as an alternative to cyclosporin in resistant cases or in patients who develop unacceptable adverse effects.
   - *b. Dose* is 0.05–0.15 mg/kg per day.
   - *c. Side effects* include nephrotoxicity, gastrointestinal disturbance, hyperglycaemia and neurological problems.
   - *d. Monitoring* involves blood pressure, renal function tests and blood glucose, initially weekly and subsequently less frequently.

Uveitis in spondylarthropathies

Ankylosing spondylitis

Ankylosing spondylitis (AS) primarily involves the sacroiliac joints and axial skeleton. About 90% of patients are positive for HLA-B27 and some have associated inflammatory bowel disease (enteropathic arthritis) (*see* Chapter 20).

Acute anterior uveitis occurs in 30% of patients with AS; conversely, 30% of males with acute iritis will have AS. Although both eyes are rarely involved simultaneously, either eye is frequently affected at different times. In severe uveitis there may be a fibrinous anterior chamber exudate. There is no correlation between the severity and activity of eye and joint involvement. Despite the high rate of recurrence, the long-term visual prognosis is good and vision-threatening complications rare. In a few patients with many recurrent attacks the inflammation may eventually become chronic.

Reiter syndrome

Reiter syndrome is defined as an episode of peripheral arthritis of more than 1 month's duration occurring in association with urethritis or cervicitis, or both. About 70% of patients are positive for HLA-B27 and 60% have associated sacroiliitis (*see* Chapter 20).

1. **Acute anterior uveitis** occurs in about 20% of patients.
2. **Bilateral mucopurulent conjunctivitis** is the most common manifestation. It usually follows the urethritis by

Fig. 10.22
Keratitis in Reiter syndrome

about 2 weeks and precedes the arthritis. It usually resolves spontaneously within 7–10 days and does not require treatment. Cultures for bacteria are usually negative.

3. **Punctate epithelial keratitis** with subepithelial infiltrates may occur in isolation or in association with conjunctivitis (Fig. 10.22).

Psoriatic arthritis

Psoriatic arthritis affects about 7% of patients with psoriasis and is associated with an increased prevalence of HLA-B27 and HLA-B17 (*see* Chapter 20).

1. **Anterior uveitis**, which may be acute or chronic, is uncommon.
2. **Conjunctivitis** occurs in some patients.
3. **Keratitis** in the form of raised marginal corneal infiltrates develops in some patients with acute iritis.
4. **Secondary Sjögren syndrome** is uncommon.

Uveitis in juvenile arthritis

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is an uncommon, inflammatory arthritis of at least 6 weeks duration developing in children before the age of 16 years. Patients are seronegative for IgM rheumatoid factor. Based on the onset and the extent of joint involvement during the first 6 months, three modes of presentation are recognized: (a) *pauciarticular*, (b) *polyarticular* and (c) *systemic* (*see* Chapter 20). The main ocular manifestation is chronic anterior uveitis. Uveitis does not occur in patients with systemic onset JIA and is uncommon in polyarticular disease. At highest risk are children with early-onset pauciarticular involvement who are also positive for antinuclear antibodies (ANA) and carriers of HLA-DR5 in whom the incidence of uveitis is approximately 20%.

> ***NB:*** JIA is not synonymous with juvenile rheumatoid arthritis. The latter is the juvenile equivalent of adult rheumatoid arthritis and is not associated with uveitis.

Clinical features

The uveitis is chronic, non-granulomatous and bilateral in 70% of cases. It is unusual for unilateral uveitis to become bilateral after more than a year. When bilateral, the severity of inflammation is usually symmetrical.

1. **Presentation** is invariably asymptomatic; the uveitis is frequently detected on routine slit-lamp examination. Even during acute exacerbations with +4 aqueous cells, it is rare for patients to complain, although a few report an increase in floaters.
2. **Signs**
   - Uninjected eye even in the presence of severe uveitis.
   - Small to medium-size KP.
   - During acute exacerbations, the entire endothelium shows 'dusting', but hypopyon does not develop.
   - Posterior synechiae are common in long-standing undetected uveitis.
3. **Prognosis**
   - In about 10% of cases the uveitis is mild, with never more than +1 aqueous cells, and persists for less than 12 months.
   - About 15% of patients have one attack, which lasts less than 4 months, the severity of inflammation varying from +2 to +4 aqueous cells.
   - In 50% of cases, the uveitis is moderate to severe and persists for more than 4 months.
   - In 25% of cases, the uveitis is very severe, lasts for several years and responds poorly to treatment. In this subgroup, band keratopathy (Fig. 10.23) occurs in 40% of patients, cataract in 30% (Fig. 10.24) and secondary inflammatory glaucoma in 15%.

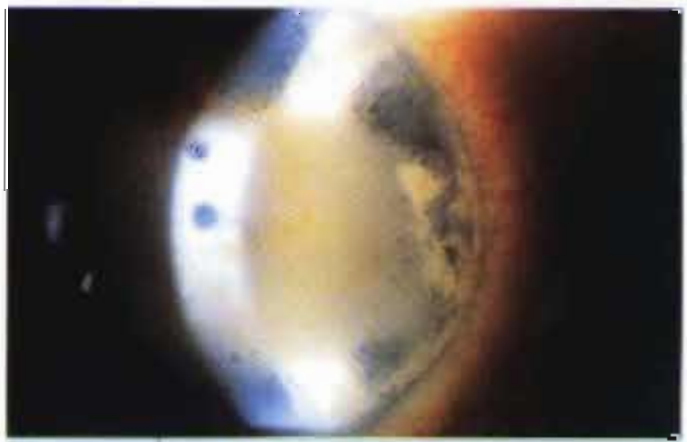


Fig. 10.23
Band keratopathy due to chronic anterior uveitis in juvenile idiopathic arthritis

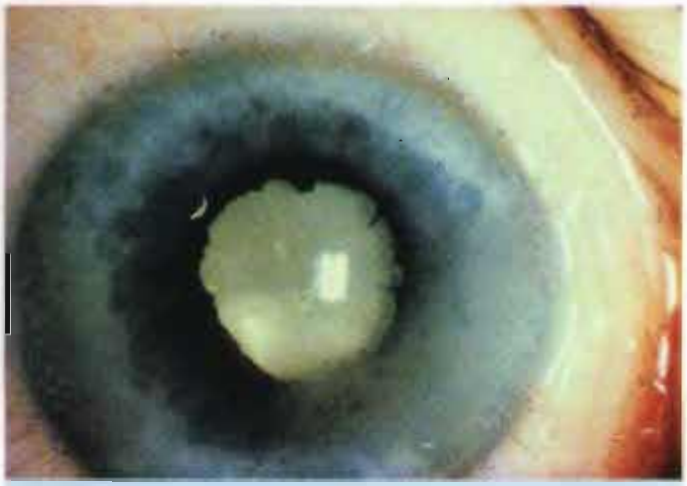


Fig. 10.24
Band keratopathy and cataract due to chronic anterior uveitis in juvenile idiopathic arthritis

Treatment

Topical steroids are usually effective: acute exacerbations require very frequent instillation. Poor responders to topical administration may benefit from periocular injections. Low-dose methotrexate is useful for steroid resistance.

Screening

Because the onset of intraocular inflammation is invariably asymptomatic, it is extremely important to regularly screen children at risk for at least 7 years from the onset of arthritis. The frequency of slit-lamp examination is governed by the various risk factors:

- Systemic onset = not required.
- Polyarticular onset = every 9 months.
- Polyarticular onset + ANA = every 6 months.
- Pauciarticular onset = every 4 months.
- Pauciarticular onset + ANA = every 3 months.

Other types of juvenile arthritis and uveitis

1. **Juvenile ankylosing spondylitis** is uncommon and typically affects boys around the age of 10 years. In contrast to adult AS, children tend to present with peripheral joint involvement but, like adults, some develop recurrent acute anterior uveitis.
2. **Juvenile Reiter syndrome** is rare and invariably post-dysenteric. A few cases of acute anterior uveitis have been reported.
3. **Juvenile psoriatic arthritis** is uncommon and may occasionally be associated with chronic anterior uveitis.
4. **Sarcoidosis** is rare in children and may present with arthropathy and anterior uveitis.
5. **Chronic infantile neurological cutaneous and articular/neonatal-onset multi-system inflammatory disease syndrome** (CINCA/NOMID) is a rare, idiopathic disease characterized by skin rash, arthropathy and involvement of the central nervous system. About 50% of children develop recurrent anterior uveitis.
6. **Lyme disease** (*see* Chapter 20).

Uveitis in inflammatory bowel disease

Ulcerative colitis

Ulcerative colitis is an idiopathic, chronic, relapsing disease involving the rectum and colon (*see* Chapter 20).

1. **Acute anterior uveitis** occurs in about 5% of patients and may synchronize with exacerbation of colitis. As expected, uveitis is commoner in patients with associated ankylosing spondylitis.
2. **Other manifestations**, which are uncommon, include peripheral corneal infiltrates, conjunctivitis and papillitis.

Crohn disease

Crohn disease is an idiopathic, chronic, relapsing disease most frequently involving the ileocaecal region (*see* Chapter 20).

1. **Acute anterior uveitis** occurs in about 3% of patients.
2. **Other manifestations,** occasionally encountered include conjunctivitis, episcleritis, peripheral corneal infiltrates and retinal periphlebitis.

Whipple disease

Whipple disease is a rare, bacterial, multi-system disease characterized by intestinal malabsorption and steatorrhoea.

1. **Uveitis** in the form of chronic iridocyclitis, vitritis and retinitis is rare.
2. **Other manifestations** include retrobulbar neuritis and other neuro-ophthalmic features.

Uveitis in nephritis

Tubulointerstitial nephritis

Tubulointerstitial nephritis and uveitis (TINU) is an uncommon hypersensitivity reaction, usually to a drug such as an antibiotic or a NSAID. It most frequently affects women and children. Renal disease usually precedes the uveitis.

1. **Presentation** is with constitutional symptoms, proteinuria, anaemia, hypertension and non-oliguric renal failure. The response to systemic steroid therapy is good and the condition resolves within a few months.
2. **Anterior uveitis**, usually bilateral, often becomes chronic and steroid-resistant. Immunosuppressive agents, however, are usually effective.

IgA glomerulonephritis

IgA glomerulonephritis is a common renal disease in which IgA is found in the glomerular mesangium.

1. **Presentation** is usually in the third to fifth decades with recurrent macroscopic haematuria which may be associated with upper respiratory tract infection.
2. **Ocular manifestations**, which are uncommon, include anterior uveitis, keratoconjunctivitis and scleritis.

Uveitis in non-infectious multi-system diseases

Sarcoidosis

Sarcoidosis is an idiopathic, granulomatous disease with frequent ocular manifestations (*see* Chapter 20). Uveitis occurs independently of the activity or severity of systemic disease, most commonly preceding or within 1 year of the onset of sarcoidosis.

Fig. 10.25
Iris nodules in sarcoid granulomatous anterior uveitis

Fig. 10.26
Snowball opacities in sarcoid intermediate uveitis

Anterior uveitis

1. **Acute** anterior uveitis typically affects patients with acute-onset sarcoid. It can usually be controlled with topical treatment.
2. **Chronic granulomatous** anterior uveitis typically affects older patients with chronic pulmonary sarcoid and is characterized by mutton fat keratic precipitates and iris nodules (Fig. 10.25). Severe and long-standing inflammation may lead to secondary cataract, glaucoma, band keratopathy and cystoid macular oedema. Periocular or systemic steroids are often required.

Intermediate uveitis

Relatively uncommon, this is characterized by vitreous cells and snowball opacities (Fig. 10.26). Treatment is initially with posterior sub-Tenon steroids. Since sarcoidosis does not invariably produce systemic manifestations, it is important to rule out this possibility in patients with presumed idiopathic intermediate uveitis.

Posterior uveitis

The posterior segment is involved in about 25% of patients with ocular sarcoid.

1. **Retinal periphlebitis** may vary in severity from mild (Fig. 10.27) to severe (Fig. 10.28). Occasionally severe periphlebitis may be associated with perivenous exudates referred to as 'candlewax drippings' (Fig. 10.29) and

Fig. 10.27
Mild sarcoid periphlebitis (Courtesy of P. Morse)

Fig. 10.28
Severe sarcoid periphlebitis

Fig. 10.30
Small choroidal sarcoid granulomas

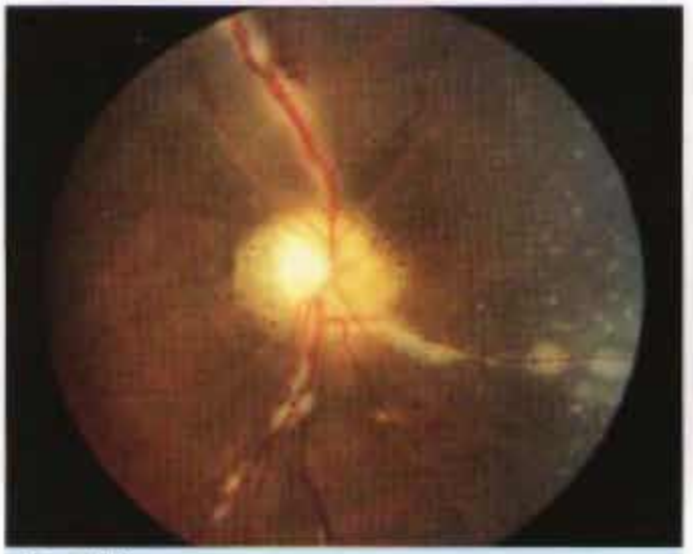


Fig. 10.29
'Candlewax drippings' in sarcoid periphlebitis (Courtesy of P. Morse)

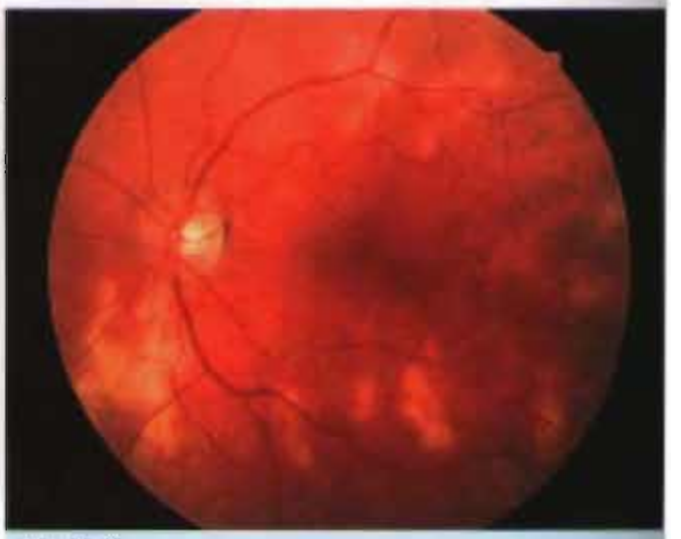


Fig. 10.31
Confluent choroidal sarcoid infiltrates

branch retinal vein occlusion. Although acute lesions may resolve spontaneously or with systemic steroids, vascular sheathing, once established, is permanent.

2. **Choroidal** granulomas are relatively uncommon and vary in appearance:
   - Multiple, small, pale-yellow infiltrates (Fig. 10.30).
   - Larger, confluent infiltrates with amoeboid margins are less common (Figs 10.31 and 10.32).
   - Large solitary choroidal granuloma (Fig. 10.33) is the least common and may be mistaken for an amelanotic choroidal melanoma.
3. **Retinal** granulomas are relatively uncommon and appear as white or yellow lesions (Fig. 10.34).
4. **Preretinal** granulomas, also uncommon, are typically located inferiorly, anterior to the equator (Landers sign) (Fig. 10.35).
5. **Optic disc granulomas** are rare and do not usually affect vision (Fig. 10.36).
6. **Peripheral retinal neovascularization** is an occasional finding (Fig. 10.37) which, in black patients, may be mistaken for that associated with sickle-cell retinopathy (*see* Chapter 14).

> ***NB:*** Papilloedema, usually secondary to involvement of the central nervous system, may occur in the absence of other eye lesions.

Treatment of posterior uveitis

Steroids are the mainstay of treatment. Prolonged steroid therapy is, however, often poorly tolerated, necessitating steroid-sparing options such as low-dose methotrexate which is a relatively safe and effective adjunct in chronic disease.

Fig. 10.32
Confluent parapapillary choroidal sarcoid granulomatous infiltration

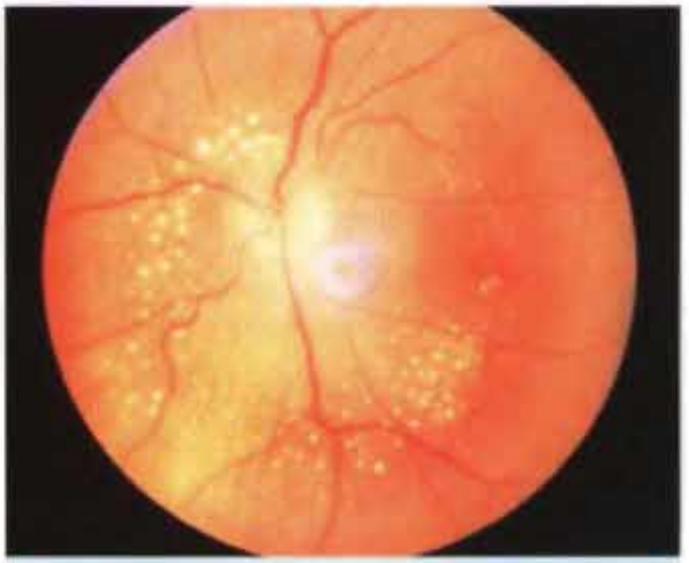


Fig. 10.34
Multiple retinal sarcoid granulomas

Fig. 10.33
Large solitary choroidal sarcoid granuloma

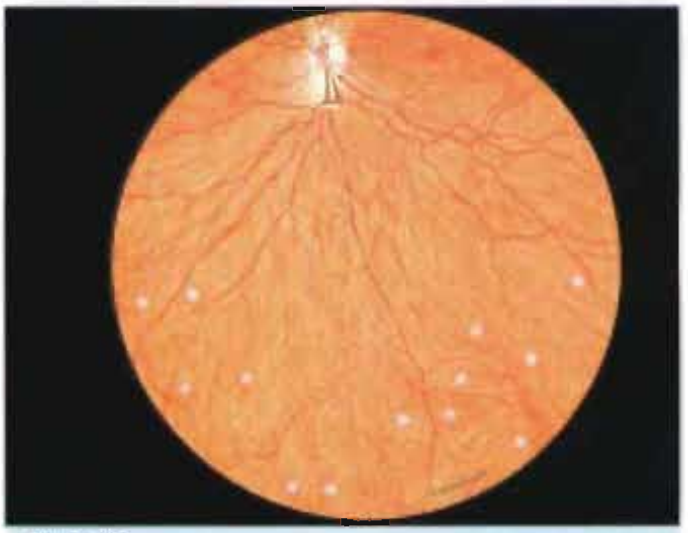
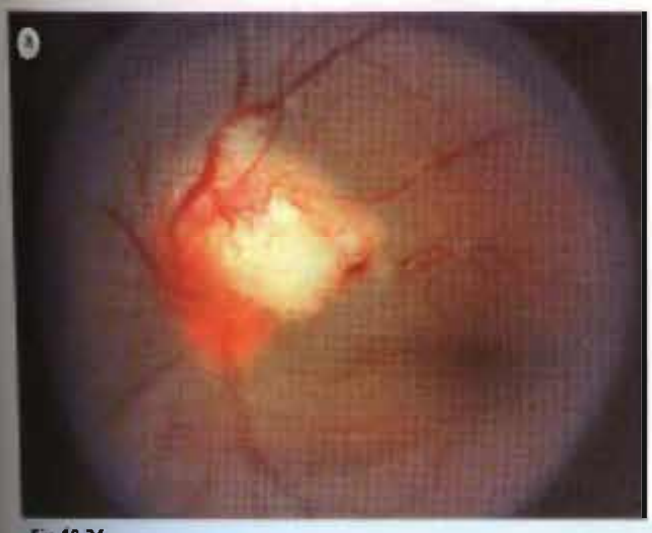


Fig. 10.35
Multiple preretinal sarcoid granulomas (Landers sign)



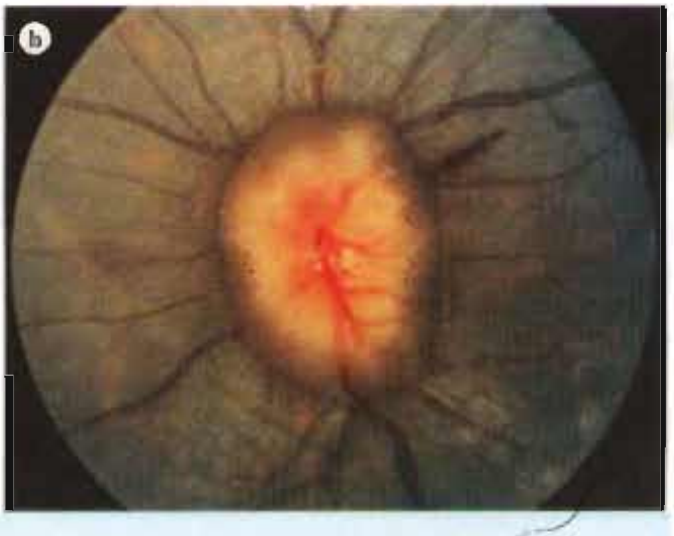


Fig. 10.36
Optic disc sarcoid granulomas (Courtesy of Wilmer Institute)

Fig. 10.37
Peripheral retinal neovascularization in sarcoidosis (Courtesy of P. Morse)

Differential diagnosis

1. **Intermediate uveitis** may be idiopathic or associated with Lyme disease, multiple sclerosis, non-Hodgkin large B-cell lymphoma and Whipple disease.
2. **Small choroidal lesions** also occur in multifocal choroiditis with panuveitis, birdshot chorioretinopathy and tuberculosis.
3. **Periphlebitis** also occurs in Behçet disease, tuberculosis, multiple sclerosis, cytomegalovirus retinitis, cat-scratch fever and Crohn disease.

Behçet disease

Behçet disease is an idiopathic disease which typically affects young men from the eastern Mediterranean region and Japan (*see* Chapter 20). Ocular manifestations, frequently bilateral, are seen in up to 95% of men and 70% of women. They usually follow, occasionally precede and rarely coincide with the onset of systemic symptoms.

Clinical features

1. **Presentation** is in the third to fourth decades with anterior or posterior uveitis.
2. **Acute recurrent anterior uveitis** may be simultaneously bilateral and is frequently associated with a transient mobile hypopyon (Fig. 10.38). Initially it responds well to topical steroids but subsequent chronicity may eventually lead to phthisis bulbi (Fig. 10.39).
3. **Retinitis** characterized by scattered, white, superficial infiltrates may occur during the acute stage of the systemic disease (Fig. 10.40). The lesions are usually transient and heal without scarring.
4. **Retinal vasculitis** may involve both veins (periphlebitis) and arteries (periarteritis) and result in vascular occlusions and macular ischaemia (Fig. 10.41).
5. **Generalized vascular leakage** may give rise to diffuse retinal or optic disc oedema (Fig. 10.42).
6. **Masssive retinal exudation** involving the outer retinal layers, with associated vascular obliteration, is rare but serious (Fig. 10.43).
7. **Vitritis**, which may be severe and persistent, is universal.

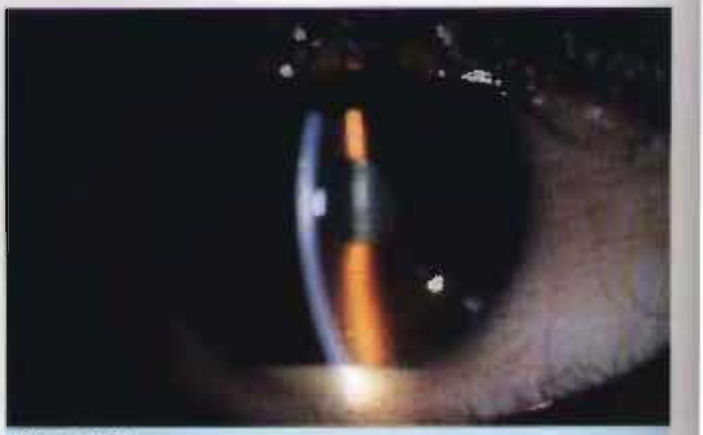


Fig. 10.38
Hypopyon in Behçet disease (Courtesy of B. Noble)

Fig. 10.39
Phthisis bulbi secondary to recurrent anterior uveitis in Behçet disease

Fig. 10.40
Retinitis in Behçet disease (Courtesy of S. Milewski)

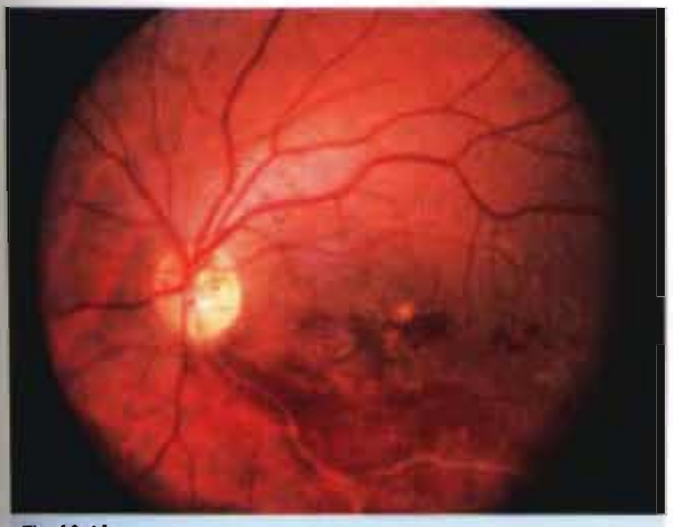


Fig. 10.41
Occlusive retinal vasculitis in Behçet disease

Fig. 10.42
Diffuse retinal oedema in Behçet disease (Courtesy of B. Noble)

Fig. 10.43
Massive retinal exudation and vascular obliteration in Behçet disease

Treatment of posterior uveitis

Posterior uveitis is treated with high-dose systemic steroids. Unfortunately, the inflammation frequently becomes steroid-resistant and requires alternative therapy with drugs such as cyclosporin, colchicine, azathioprine, chlorambucil and levamisole, which are also useful for the systemic manifestations of the disease. Despite treatment, 5–10% of patients become blind. The end stage of posterior segment involvement is characterized by optic atrophy, vascular attenuation and sheathing, and variable chorioretinal scarring (Fig. 10.44).

NB: A recent study suggests that a single intravenous infusion of infliximab, a drug used for rheumatoid arthritis, is safe and highly effective.

Differential diagnosis

In patients with incomplete or atypical forms of Behçet disease the diagnosis may be uncertain because there are no definitive laboratory tests. It is therefore important to consider the following conditions:

1. **Recurrent anterior uveitis with hypopyon** may be associated with spondylarthropathies. However, such uveitis is not usually simultaneously bilateral. Moreover, the hypopyon is not mobile because it is frequently associated with a fibrinous exudate. In Behçet disease the hypopyon shifts with gravity when head posture changes.
2. **Retinal infiltrates** similar to those in Behçet disease may be seen in viral retinitides such as the acute retinal necrosis syndrome, in which, however, the infiltrates eventually coalesce. Multiple retinal infiltrates also occur in idiopathic acute multifocal retinitis. In contrast to

Fig. 10.44
End-stage vascular occlusion, retinal scarring and consecutive optic atrophy in Behçet disease

Behçet disease the clinical course is favourable, with return to normal vision within 2-4 months.

Vogt–Koyanagi–Harada syndrome

The Vogt–Koyanagi–Harada (V-K-H) syndrome is an idiopathic, bilateral, granulomatous panuveitis associated with systemic manifestations (*see* Chapter 20). In practice, the condition can be subdivided into Vogt–Koyanagi syndrome characterized mainly by cutaneous manifestations and anterior uveitis, and Harada disease, in which neurological features and exudative retinal detachment predominate. V-K-H has three clinical phases: (a) *uveitic*, (b) *convalescent* and (c) *chronic–recurrent*.

Phases

1. **Uveitic** phase develops within 1–2 days of prodromal manifestations.
   a. ***Bilateral anterior uveitis***, usually granulomatous, predominates in Vogt-Koyanagi syndrome and is mild in Harada disease.

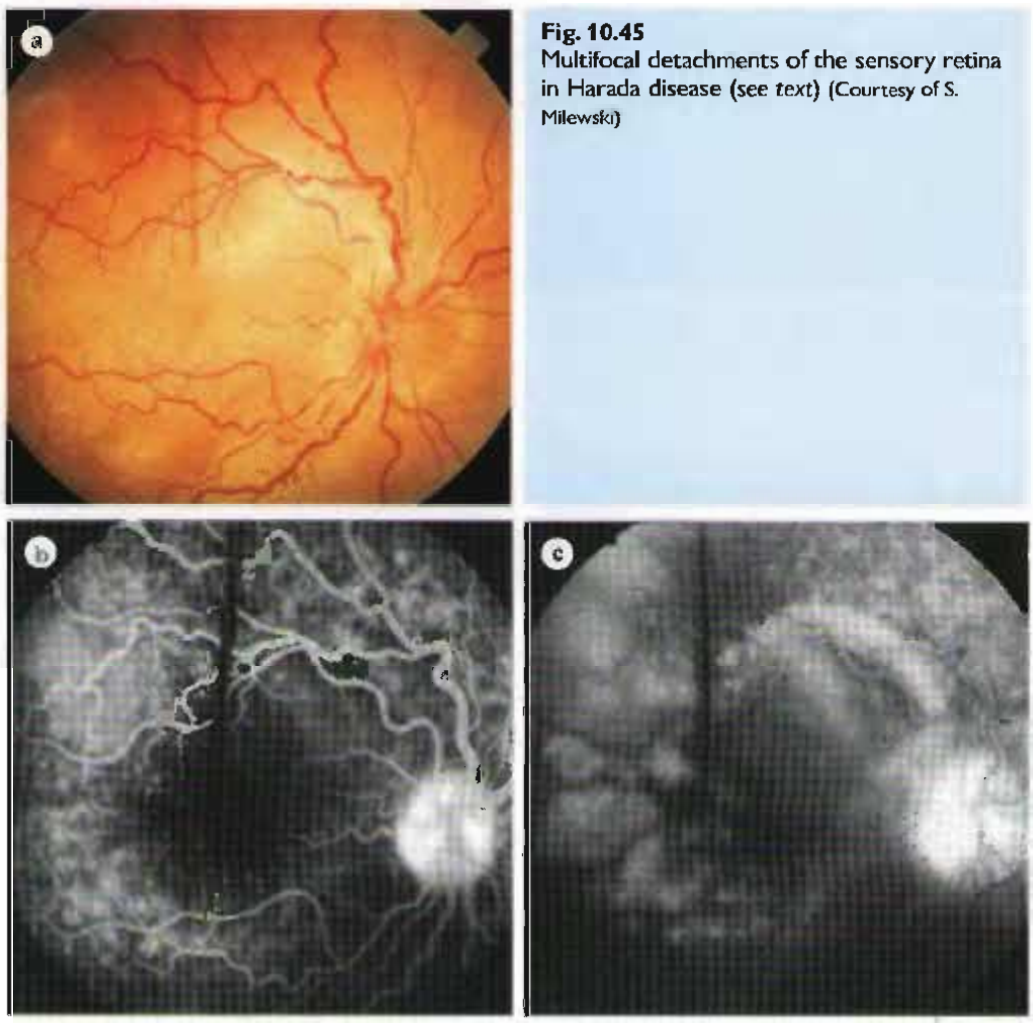


Fig. 10.45
Multifocal detachments of the sensory retina in Harada disease (see *text*) (Courtesy of S. Milewski)

Fig. 10.46
Inferior exudative retinal detachment in Harada disease

b. Bilateral posterior uveitis occurs in Harada disease and proceeds as follows:

- Optic disc oedema and multifocal detachments of the sensory retina, with small folds radiating from the macula (Fig. 10.45a). FA shows early pinpoint hyperfluorescent spots at the level of the retinal pigment epithelium (Fig. 10.45b), which gradually enlarge as dye pools in the subretinal space (Fig. 10.45c).
- Coalescence of multifocal detachments, resulting in exudative retinal detachment (Fig. 10.46), which gradually subsides spontaneously or with systemic steroid therapy.

2. **Convalescent** phase develops about 4 weeks after the onset of uveitis.
   - Numerous, residual, small, mottled, atrophic scars ('sunset glow' fundus) (Fig. 10.47).
   - Perilimbal vitiligo (Sugiura sign) may be seen, particularly in Japanese patients.
3. **Chronic–recurrent** phase is characterized by chronic granulomatous anterior uveitis, more severe in Vogt–Koyanagi syndrome, often leading to posterior synechiae, secondary cataract and glaucoma.

Treatment

This is aimed at shortening the duration of the disease and preventing chronicity, with its associated complications. This is best achieved by early and aggressive use of systemic steroids, followed by slow tapering over 3–6 months. Steroid-resistant patients may require cyclosporin, azathioprine or chlorambucil. The prognosis is fair with 60% of patients retaining a visual acuity of at least 6/9. Uncommon posterior segment complications include choroidal neovascularization and rarely subretinal fibrosis.

Viral uveitis

Herpes zoster

The varicella zoster virus (VZV) is a herpes virus that causes chickenpox, remains latent in a primary sensory ganglion, and may subsequently reactivate, resulting in herpes zoster (shingles). Immunosuppressed organ transplant recipients and immune-deficient patients with cancer, leukaemia and AIDS are all at increased risk. In herpes zoster ophthalmicus (HZO), involvement of the tip of the nose (Hutchinson sign), supplied by the external nasal nerve (a terminal branch of the nasociliary nerve), signifies an increased risk of uveitis (Fig. 10.48). Many of the iris changes in patients with uveal involvement are thought to be due to ischaemic occlusive vasculitis.

1. **Presentation** in the vast majority of patients is with HZO, although anterior uveitis may rarely occur in patients with minimal or no cutaneous lesions (herpes zoster sine herpete), the only clue being neuralgia in the distribution of the first division of the trigeminal nerve.

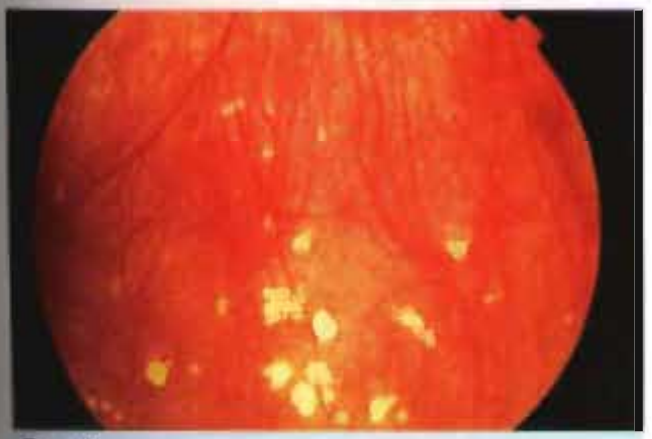


Fig. 10.47
Chorioretinal scars in Harada disease ('sunset glow' fundus)

Fig. 10.48
Involvement of the tip of the nose in herpes zoster ophthalmicus (Hutchinson sign)

Fig. 10.49
Transillumination defect due to stromal iris atrophy in herpes zoster anterior uveitis

2. **Signs**
   - Corneal sensation may be reduced and nummular keratitis may be present.
   - Keratic precipitates are frequently small and occasionally 'mutton fat'.
   - Anterior chamber activity is usually mild.
   - Iridoplegia and sectoral iris oedema.
   - Posterior synechiae are common.
3. **Complications** may occur if the uveitis is not treated vigorously.
   a. ***Iris atrophy*** is characterized by sectoral loss of the iris pigment epithelium, due to ischaemic vasculitis, resulting in transillumination defects (Fig. 10.49).
   b. ***Secondary glaucoma***, often acute, occurs in about 10% of eyes, due to combination of trabecular inflammation (trabeculitis) and obstruction by inflammatory debris.
4. **Treatment** with topical steroids needs to be continued for several months and then tapered very gradually. Some patients may require very low-dose treatment indefinitely in order to maintain long-term control of the inflammation.

NB: Although the diagnosis is usually straightforward, it is important to remember that severe uveitis may follow an almost inapparent episode of herpes zoster. The initial diagnosis may well have been missed and the patient may present months later with a florid unilateral anterior uveitis. It is therefore important always to consider the possibility of HZO and perform the following:
- Test corneal sensation because it is often reduced after HZO.
- Examine the cornea for nummular keratitis.
- Transilluminate the iris for sectoral atrophy.
- Inspect the hairline at the scalp for post-herpetic scarring and pigmentary changes.

Cytomegalovirus retinitis

Cytomegalovirus (CMV) retinitis is the most common ocular infection in AIDS patients and on rare occasions may be the initial manifestation of the disease (*see* Chapter 20). Before the advent of highly active antiretroviral therapy (HAART), CMV retinitis affected 30% of patients with AIDS at some time during the course of their disease. Since the introduction of HAART the incidence of CMV retinitis has substantially decreased.

Clinical features

1. **Indolent retinitis** frequently starts in the periphery and progresses slowly. It is characterized by mild granular opacification (Fig. 10.50).
2. **Fulminating retinitis** (in chronological order)
   - Dense, white, geographical area of opacification associated with vasculitis and mild vitritis (Fig. 10.51).
   - Gradual spread associated with haemorrhage (Fig. 10.52)

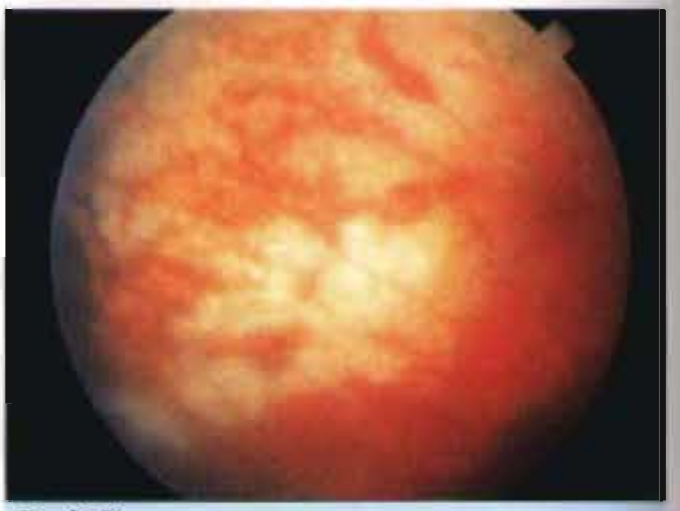


Fig. 10.50
Indolent CMV retinitis

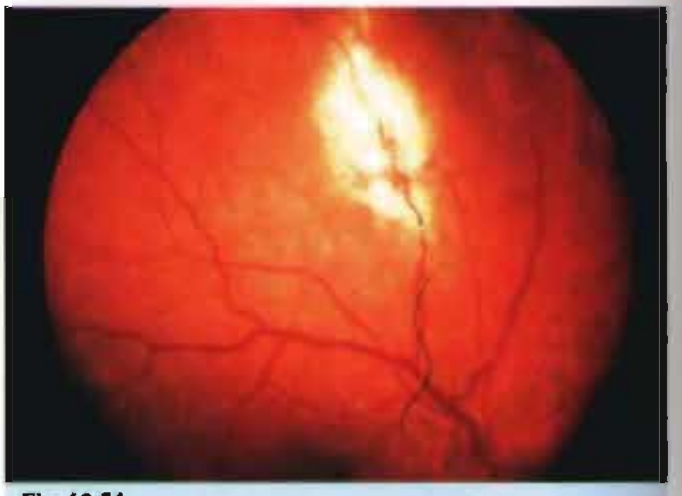


Fig. 10.51
Early fulminating CMV retinitis

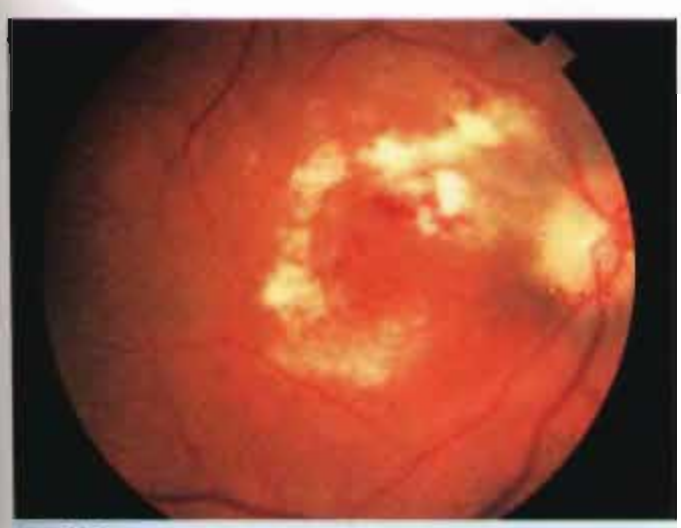


Fig. 10.52
Fulminating CMV retinitis

- Slow but relentless 'brushfire-like' extension along the retinal blood vessels (Fig. 10.53) and involvement of the optic nerve head (Fig. 10.54).
- Without treatment blindness ensues within several weeks to a few months from extensive retinal involvement (Fig. 10.55), retinal detachment or consecutive optic atrophy.

3. **Regression** following treatment is characterized by fewer haemorrhages, less opacification, and diffuse atrophic and pigmentary changes (Fig. 10.56).

Treatment

Retinal detachment is frequently amenable to vitrectomy and silicone oil tamponade. The following drugs may be used individually or in combination to treat active CMV.

1. **Systemic ganciclovir** is initially administered intravenously, 10 mg/kg every 12 hours for 2–3 weeks (induction), and subsequently at 5 mg/kg every 24 hours until

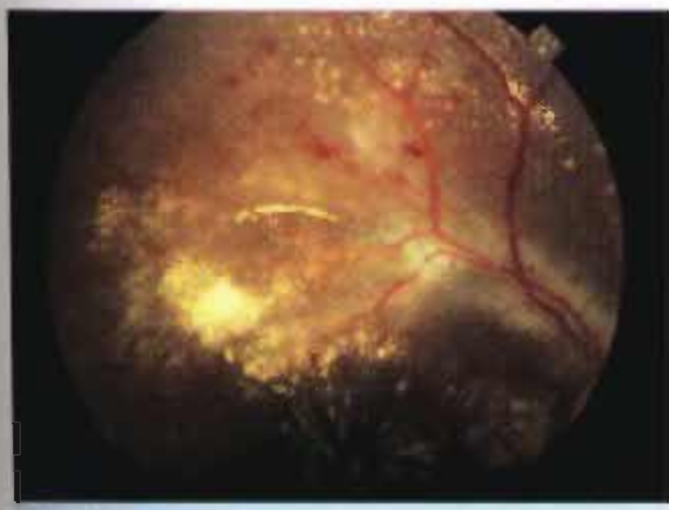


Fig. 10.53
Fulminating CMV retinitis (Courtesy of S. Milewski)

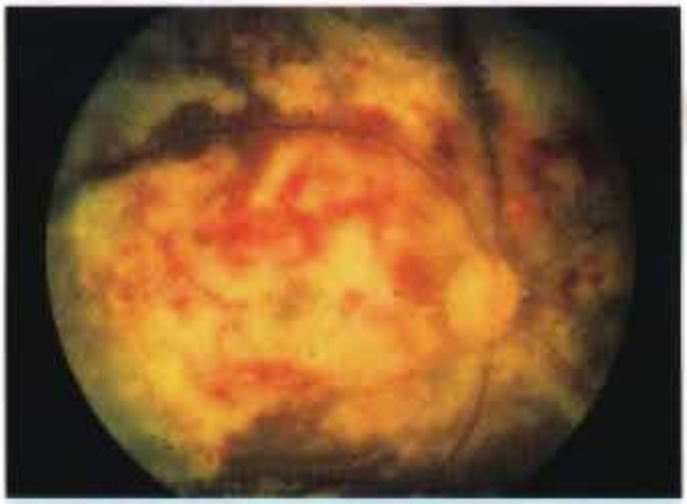


Fig. 10.55
End-stage CMV retinitis

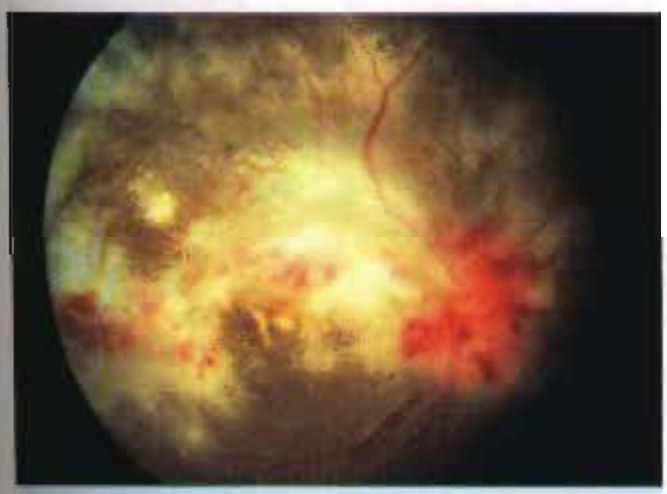


Fig. 10.54
Optic nerve head involvement by fulminating CMV retinitis (Courtesy of S. Milewski)

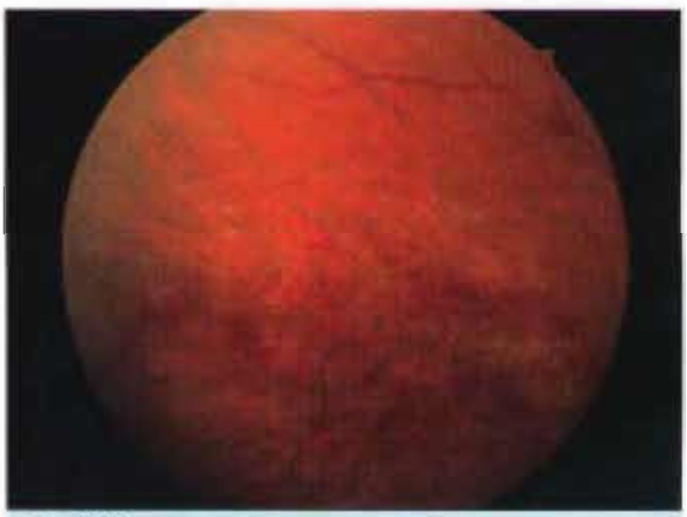


Fig. 10.56
Inactive CMV retinitis

Fig. 10.57
Slow-release intravitreal ganciclovir implant (Courtesy of V. Tanner)

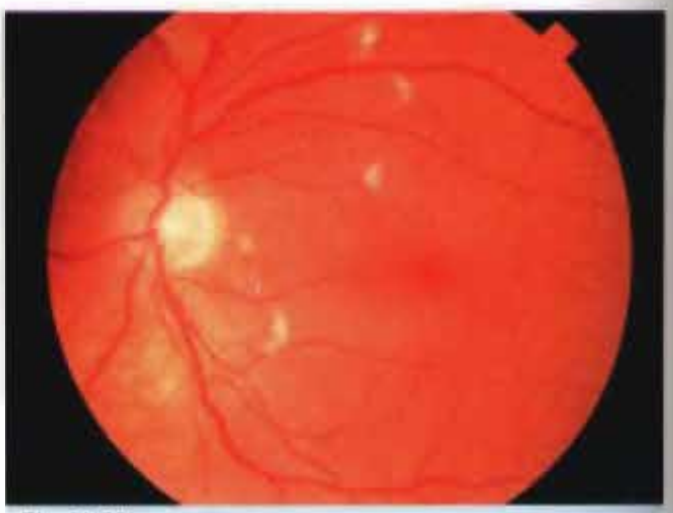


Fig. 10.58
Cotton wool spots in HIV retinopathy (Courtesy of S. Milewski)

retinitis is stable. Thereafter the lifelong oral maintenance dose is 300 mg daily. Ganciclovir is effective in 80% of patients but half of these subsequently relapse and require reinduction. The drug carries a high risk of bone marrow suppression, which often forces interruption of treatment.

2. **Intravitreal ganciclovir**, by injection or a slow-release device (Vitrasert, duration of action 8 months) (Fig. 10.57), is as effective as intravenous therapy. However, this fails to protect the fellow eye and is less effective in treating recurrences in patients previously treated with intravenous ganciclovir. Intravitreal injections may also cause serious complications such as vitreous haemorrhage, retinal detachment and endophthalmitis.
3. **Foscarnet** administered intravenously, 60 mg/kg every 8 hours for 2–3 weeks and then daily, is an alternative to ganciclovir. Side effects include nephrotoxicity, electrolyte disturbances and seizures. Foscarnet can also be given intravitreally.
4. **Cidofovir** administered intravenously, 5 mg/kg once weekly for 2 weeks and then every 2 weeks, in combination with probenecid, may be used where other agents are unsuitable. Side effects include nephrotoxicity, neutropenia and uveitis. Cidofovir can also be given intravitreally.

Prognosis

With treatment there is an initial 95% response but relapse is invariable within 2 weeks if treatment is discontinued. The relapse rate within 6 months in patients on maintenance therapy is 50%. Patients who demonstrate a sustained HAART-induced immune recovery with elevation of CD4+ cell count are more likely to remain quiescent for a longer period of time if anti-CMV therapy is withdrawn. However, such patients may develop transient but severe vitreous inflammation which probably reflects an improved anti-CMV immune response.

Other types of uveitis in AIDS

The following types of uveitis may occur in AIDS in the absence of opportunistic infections:

1. **HIV-induced** retinal microangiopathy is characterized by multiple, usually asymptomatic cotton wool spots (Fig. 10.58) which resolve spontaneously.
2. **Cidofovir-induced** uveitis responds well to conventional treatment with topical steroids and may not preclude continuation of cidofovir.
3. **Rifabutin-induced** uveitis in patients treated for *Mycobacterium avium* complex infections.
4. **Immune recovery** uveitis is a paradoxical worsening of intraocular inflammation, mainly vitritis, in patients with HAART-induced immune recovery who also have inactive CMV retinitis. Complications include cataract, cystoid macular oedema and epiretinal gliosis.
5. **Chronic multifocal retinal infiltrates** associated with anterior uveitis or vitritis are rare. The uveitis responds well to steroids and the retinitis to zidovudine. Visual prognosis is good.

Progressive outer retinal necrosis

Progressive outer retinal necrosis (PORN) is a devastating condition caused by an aggressive variant of varicella zoster virus and is the second most common opportunistic retinal infection in AIDS.

1. **Presentation** is with rapidly progressive visual loss which is often initially unilateral and then becomes bilateral.
2. **Signs** (in chronological order)
   - Multifocal, deep, yellow-white, retinal infiltrates with minimal vitritis.
   - Rapid confluence, full-thickness retinal necrosis and early macular involvement (Fig. 10.59).
3. **Investigations**. Specific PCR-based diagnostic assay for varicella zoster virus DNA may be performed on vitreous samples to confirm the diagnosis.
4. **Treatment** is with intravenous ganciclovir alone or in combination with foscarnet. Despite treatment, most patients become blind in both eyes within a few weeks as a

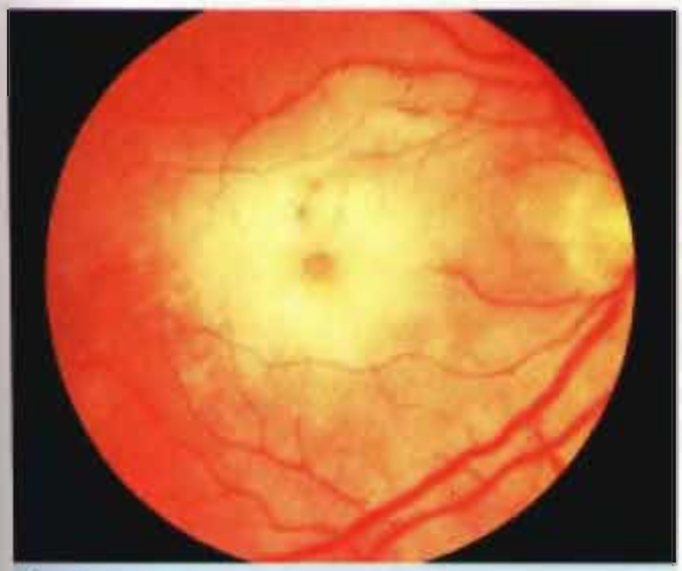


Fig. 10.59
Macular involvement in progressive outer retinal necrosis
(Courtesy of S. Mitchell)

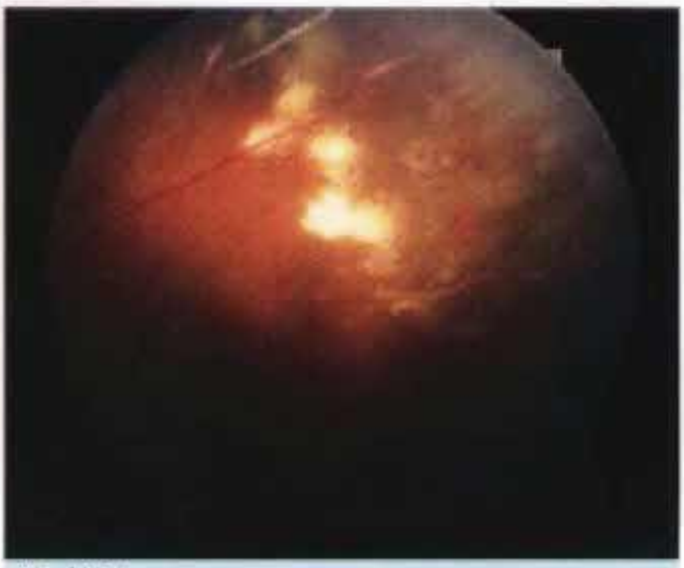


Fig. 10.61
Early acute retinal necrosis

result of macular necrosis or retinal detachment. In addition 50% are dead 5 months after the diagnosis. The results of retinal surgery are disappointing, although vitrectomy with silicone oil tamponade and relaxing retinotomy may salvage ambulatory vision in a few cases.

Acute retinal necrosis

Acute retinal necrosis (ARN) is a rare but devastating necrotizing retinitis, typically affecting otherwise healthy individuals of all ages. The actiology is biphasic: due to herpes simplex virus 2 under the age of 15 years and to varicella zoster virus and herpes simplex virus 1 in older individuals. It is twice as common in males.

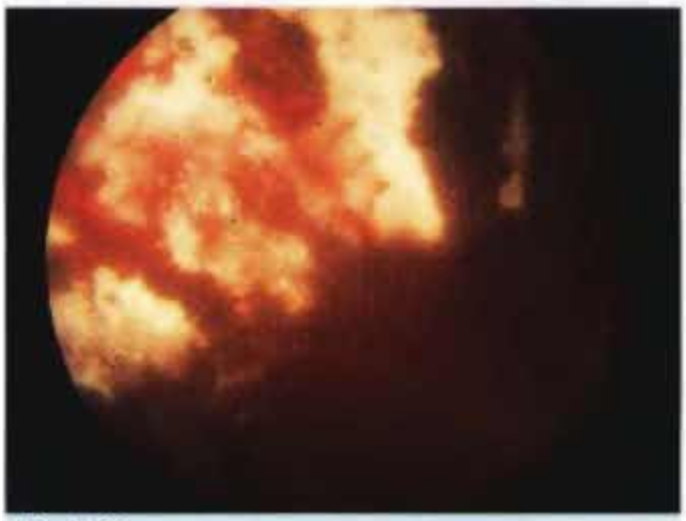


Fig. 10.62
Advanced acute retinal necrosis

Fig. 10.60
Vitritis in acute retinal necrosis

Clinical features

1. **Presentation** is variable. Some patients develop painful severe visual impairment over a few days, while others have an insidious onset with mild visual symptoms such as floaters.
2. **Signs** (in chronological order)
   - Anterior granulomatous uveitis and vitritis (Fig. 10.60) are universal; unless the fundus is examined the diagnosis may be missed.
   - Peripheral retinal periarteritis and multifocal, deep, yellow-white, retinal infiltrates (Fig. 10.61).
   - Gradual confluence of the lesions (Fig. 10.62) and the development of full-thickness retinal necrosis.

Fig. 10.63
Advanced acute retinal necrosis

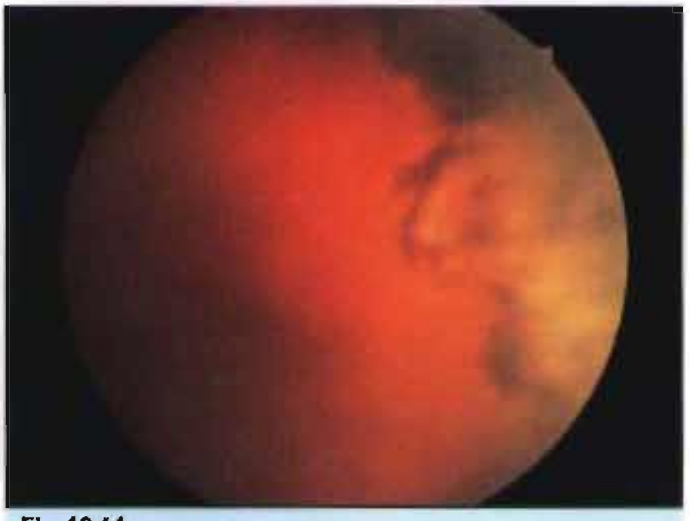


Fig. 10.64
Resolved acute retinal necrosis

- The posterior pole is usually spared until late. Visual acuity may therefore remain fairly good despite necrosis of the surrounding retina (Fig. 10.63).
- Other signs include optic disc oedema, choroidal thickening and retinal haemorrhages.

3. **Investigations.** PCR-based assays of aqueous and vitreous are very helpful in confirming the diagnosis and determination of the causative virus.
4. **Course.** The retinitis resolves within 6–12 weeks, leaving behind necrotic retina with hyperpigmented borders (Fig. 10.64). Without appropriate treatment the second eye becomes involved in about 65% of cases, usually within 6–14 weeks of the first. The prognosis with treatment is guarded, with a final visual acuity of 6/12 or better in 50% of cases. Complications include retinal detachment, which may be rhegmatogenous or tractional, anterior ischaemic optic neuropathy and retinal vascular occlusion.

Treatment

1. **Aciclovir** initially intravenously for 14 days (10 mg kg per day in three divided doses) and then orally for 3 months (800 mg five times daily). There may be no signs of improvement for up to 5 days after starting therapy. Treatment also reduces but does not eliminate the risk of fellow eye involvement.
2. **Famciclovir** orally 500 mg t.i.d. for 3 months may be helpful in patients unresponsive to aciclovir.
3. **Systemic steroids** are started a few days after initiation of antiviral therapy.
4. **Aspirin** may be used in an effort to prevent vascular obstructive complications.
5. **Prophylactic** argon laser photocoagulation, to create a chorioretinal adhesion in areas of potential retinal break formation, may be effective in preventing retinal detachment if applied early.
6. **Vitreoretinal surgery**, including silicone oil tamponade, may be successful for complicated retinal detachments.

Congenital rubella

Rubella (German measles) is a benign febrile exanthema. Congenital rubella results from transplacental transmission of virus to the fetus from an infected mother, usually during the first trimester of pregnancy, resulting in serious chronic fetal infection and malformations. The risk to the fetus is related to the stage of gestation at the time of maternal infection, being highest in the first 8 weeks of pregnancy. In order of frequency, ocular complications are as follows:

1. **Retinopathy** is characterized by a visually insignificant, subtle 'salt and pepper' pigmentary disturbance, most marked at the macula (Fig. 10.65). A small percentage of cases may later develop choroidal neovascularization.
2. **Pearly nuclear cataract** may be unilateral or bilateral. Cataract surgery may be associated with a florid intractable uveitis.

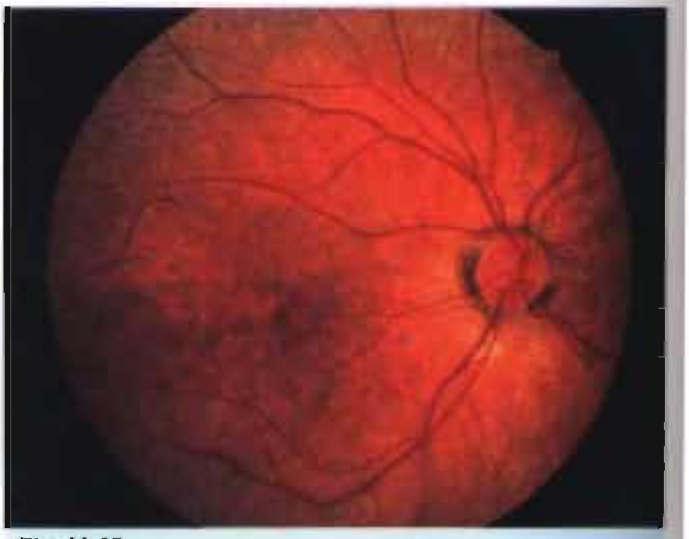


Fig. 10.65
Rubella retinopathy

Fig. 10.66
Left microphthalmos in rubella

3. **Microphthalmos** (Fig. 10.66) is often associated with cataracts, optic nerve abnormalities and glaucoma.
4. **Glaucoma** develops usually during the neonatal period, resulting in buphthalmos. However, in a microphthalmic eye, the raised intraocular pressure may enlarge the cornea to normal size. Corneal oedema is also an important feature of glaucoma.
5. **Miscellaneous** complications include stromal keratopathy, iritis, iris atrophy and extreme refractive errors. Pendular nystagmus and strabismus may develop as a consequence of the various ocular abnormalities.

Parasitic uveitis

Toxoplasma retinitis

Toxoplasma gondii is an obligate intracellular protozoan. The cat is the definitive host and other animals, such as mice, livestock and humans, are intermediate hosts. The parasite has three forms: (a) *sporocysts* (oocysts), which are excreted in cat faeces, (b) *bradyzoites*, which are encysted in tissue, and (c) *tachyzoites*, which proliferate and cause tissue destruction. Toxoplasmosis is the most frequent cause of infectious retinitis in immunocompetent individuals. Although most cases are thought to represent reactivation of prenatal infestation it is likely that postnatally acquired toxoplasma retinitis may be more frequent than previously realized. Recurrent episodes, usually between the ages of 10 and 35 years, are common and occur when the cysts rupture, releasing hundreds of tachyzoites into adjacent normal retinal cells. The scars from which recurrences arise may be the residue of previous congenital infestation or, less frequently, remote acquired involvement. Active retinitis is usually associated with anterior uveitis which may be non-granulomatous or granulomatous. It is therefore very important to examine the fundus in all patients with anterior uveitis.

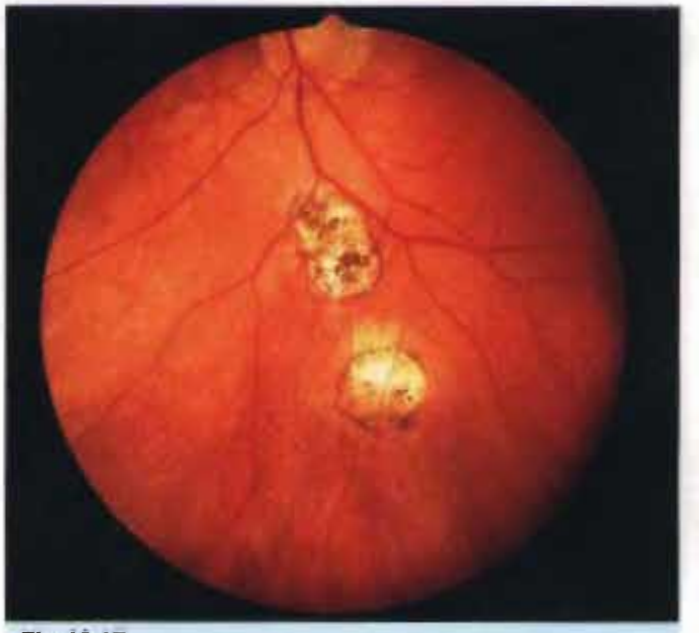


Fig. 10.67
Peripheral chorioretinal scars due to toxoplasmosis

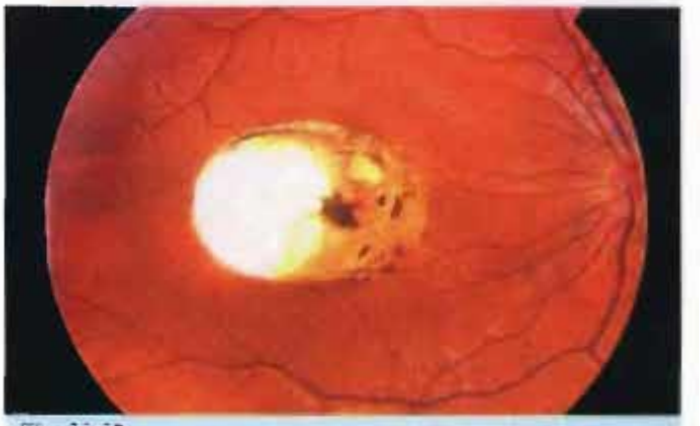


Fig. 10.68
Macular scarring due to toxoplasmosis

Signs

1. **Quiescent** healed lesions are foci of chorioretinal atrophy and scarring, with pigmented borders (Fig. 10.67). They are often bilateral and often discovered incidentally, or when a child is noted to have impaired vision because of macular involvement (Fig. 10.68).
2. **Focal retinitis**
   - A solitary inflammatory focus of variable size, with overlying vitreous haze, adjacent to an old pigmented scar ('satellite lesion') is the most common finding (Fig. 10.69).
   - Severe vitritis may impair visualization of the fundus, although the inflammatory focus may still be discernible ('headlight in the fog' appearance) (Fig. 10.70).
   - Associated features include vasculitis and in some cases the detached posterior hyaloid face becomes covered by inflammatory precipitates.

Fig. 10.69
Typical toxoplasma retinitis

Fig. 10.70
Toxoplasma retinitis and severe vitritis resulting in a 'headlight in the fog' appearance

3. **Papillitis** (inflammation of the optic nerve head) may be secondary to juxtapapillary retinitis (Jensen choroiditis) (Fig. 10.71). Very occasionally, the optic nerve head may be the primary site of involvement.
4. **Atypical lesions**, which may occur in immunocompromised individuals, are characterized by bilateral, multifocal, discrete foci (Fig. 10.72) or extensive confluent areas of retinitis (Fig. 10.73). Pre-existing scars are absent, implying that the infestation has been newly acquired or disseminated to the eye from extraocular sites.

Fig. 10.71
Juxtapapillary toxoplasma retinitis

Fig. 10.72
Atypical multifocal toxoplasma retinitis in AIDS (Courtesy of J. Salmon)

Diagnostic tests

Diagnosis is based on a compatible fundus lesion and positive serology for toxoplasma antibodies. Any antibody titre is significant, there being no correlation between titre and inflammatory activity.

1. **Indirect immunofluorescent antibody** tests utilize dead organisms that are exposed to the patient's serum and anti-human globulin labelled with fluorescein. The results are interpreted under fluorescent microscopy.
2. **Haemagglutination** tests involve coating of lysed organisms on to red blood cells, which are then exposed to the patient's serum. Positive sera cause the red cells to agglutinate.

Fig. 10.73
Confluent scarring due to toxoplasmosis

3. **Enzyme-linked immunosorbent assay** (ELISA) involves binding of the patient's serum to an excess of solid-phase antigen. This complex is then incubated with an enzyme-linked second anti-human antibody. Assessment of enzyme activity provides a measure of specific antibody concentration. The test can also detect antibodies in the aqueous humour, which are more specific than those in the serum.

Indications for treatment

1. **In immunocompetent** patients not all active lesions require treatment; small peripheral foci are frequently self-limiting and innocuous. The following are the main indications for treatment:

Fig. 10.74
Toxoplasma retinitis involving the papillomacular bundle
(Courtesy of M Szreter)

- A lesion threatening or involving the macula, papillomacular bundle (Fig. 10.74), optic nerve head or a major blood vessel.
- A very severe vitritis, due to the risk of subsequent vitreous fibrosis and tractional retinal detachment.

2. **In immunocompromised** patients all lesions should be treated irrespective of location or severity.

Treatment

There is no universally agreed therapeutic regimen. Treatment influences neither the duration of inflammation nor the frequency of recurrences, although it appears to limit the ultimate size of the scar. Systemic steroids are indicated for vision-threatening lesions, particularly if associated with severe vitritis, and are administered in conjunction with one or more of the following agents. Steroids are, however, contraindicated in immunocompromised patients.

1. **Clindamycin** 300 mg q.i.d. orally for 3 weeks. If used alone, it may cause a pseudomembranous colitis. The risk of colitis is reduced when clindamycin is used together with sulphadiazine that inhibits clostridial overgrowth.
2. **Sulphadiazine**. The loading oral dose is 2 g followed by 1 g q.i.d. for 3–4 weeks. Side effects include renal stones, allergic reactions and Stevens–Johnson syndrome.
3. **Pyrimethamine** (Daraprim) is a strong anti-toxoplasma agent, which may, however, cause thrombocytopenia, leucopenia and folate deficiency. For this reason, weekly blood counts should be done and the drug used only in combination with oral folinic acid 4 mg three times a week (mixed with orange juice) to counteract side effects. The loading dose is 50 mg followed by 25–50 mg daily for 4 weeks. Pyrimethamine should not be used in patients with AIDS.
4. **Co-trimoxazole** (Septrin) (trimethoprim 160 mg and sulphamethoxazole 800 mg) 960 mg b.d. orally for 4–6 weeks, may be effective alone or in combination with clindamycin.
5. **Atovaquone** 750 mg t.i.d. has been used mainly for pneumocystosis and toxoplasmosis in AIDS but may also be effective against toxoplasma retinitis in immunocompetent individuals. The drug is relatively free of serious side effects but is expensive.
6. **Azithromycin** 500 mg daily on three successive days may be used in patients intolerant to other drugs.

Prognosis

In immunocompetent hosts, the retinitis heals within 1–4 months. The vitreous haze gradually clears although some condensation may remain. The inflammatory focus evolves into a sharply demarcated atrophic scar with a hyperpigmented border (see Fig. 10.67). Resolution of anterior uveitis is a reliable sign of posterior segment healing. After the first attack, the mean recurrence rate within 3 years is about 50% and the average number of recurrent attacks per patient is 2.7. Eyes with toxoplasmosis may lose vision from direct or indirect causes:

1. **Direct involvement** by an inflammatory focus of the fovea, papillomacular bundle, optic nerve head or a major blood vessel.
2. **Indirect involvement** by macular pucker or retinal detachment (tractional or rhegmatogenous).

Toxocariasis

Toxocariasis is caused by infestation with *Toxocara canis*, a common intestinal roundworm of dogs. Human infestation occurs secondary to ingestion of soil or food contaminated with ova shed in dogs' faeces. In the intestine, the ova develop into larvae, which penetrate the intestinal wall and travel to various organs such as the liver, lungs, skin, brain and eyes. When the larvae die, they disintegrate and cause an inflammatory reaction followed by granulation. Clinically human infestation may take one of two forms (a) *visceral larva migrans* and (b) *ocular toxocariasis*.

Unlike visceral larva migrans, which is a severe systemic infestation usually occurring around the age of 2 years, in which the eyes are spared, ocular toxocariasis occurs in otherwise healthy children. It may take one of three forms, all affecting only one eye: (a) *a chronic endophthalmitis-like picture*, (b) *posterior pole granuloma* and (c) *peripheral granuloma*. Of these, only the first is associated with active inflammation. Less common manifestations include anterior uveitis, papillitis, a localized vitreous abscess and retinal tracks.

Chronic endophthalmitis

1. **Presentation** is between 2 and 9 years of age with leukocoria, strabismus or unilateral visual loss.
2. **Signs**. Anterior uveitis and vitritis. The peripheral retina and pars plana may be covered by a dense greyish-white exudate, similar to 'snow-banking' in pars planitis (Fig. 10.75).
3. **Complications** include tractional retinal detachment, hypotony and cataract.
4. **Treatment** with periocular steroids may be helpful. Vitreoretinal surgery may be beneficial for tractional retinal detachment but in general the prognosis is very poor; some eyes eventually require enucleation.

Posterior pole granuloma

1. **Presentation** is between 6 and 14 years of age with unilateral visual impairment.

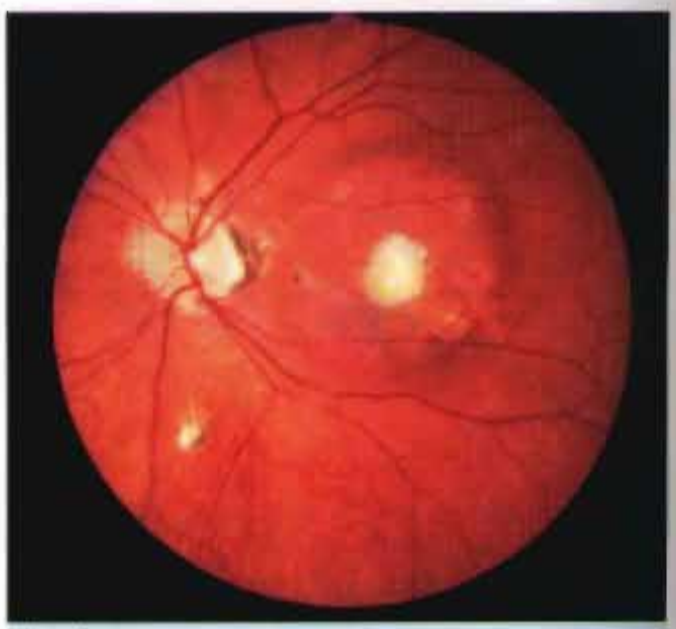


Fig. 10.76
Toxocara granuloma at the posterior pole

Fig. 10.75
Peripheral exudation in chronic toxocara endophthalmitis
(Courtesy of S. Lightman)

Fig. 10.77
Toxocara granuloma involving the optic nerve head

2. **Signs**. Absence of uveitis. A round, yellow-white, solid granuloma between one to two discs in diameter, is seen at the macula (Fig. 10.76). Occasionally it may involve the optic nerve head (Fig. 10.77).
3. **Complications** include retinal stress lines, vascular distortion, hard exudates surrounding the lesion, subretinal haemorrhage and retinal detachment (Fig. 10.78), which may be amenable to vitreoretinal surgery.

Peripheral granuloma

1. **Presentation** is usually during adolescence or adult life with visual impairment from distortion of the macula or retinal detachment. In an uncomplicated case, the lesion may remain undetected throughout life.
2. **Signs**. Absence of uveitis. A white hemispherical granuloma may be seen at or anterior to the equator in any quadrant of the fundus (Fig. 10.79). Vitreous bands frequently extend from the lesion to the posterior fundus; on contraction they may give rise to 'dragging' of the disc and straightening of blood vessels (Fig. 10.80).
3. **Complications** include macular heterotopia (abnormal position), which may result in pseudo-strabismus, and tractional retinal detachment, which may be amenable to vitreoretinal surgery.

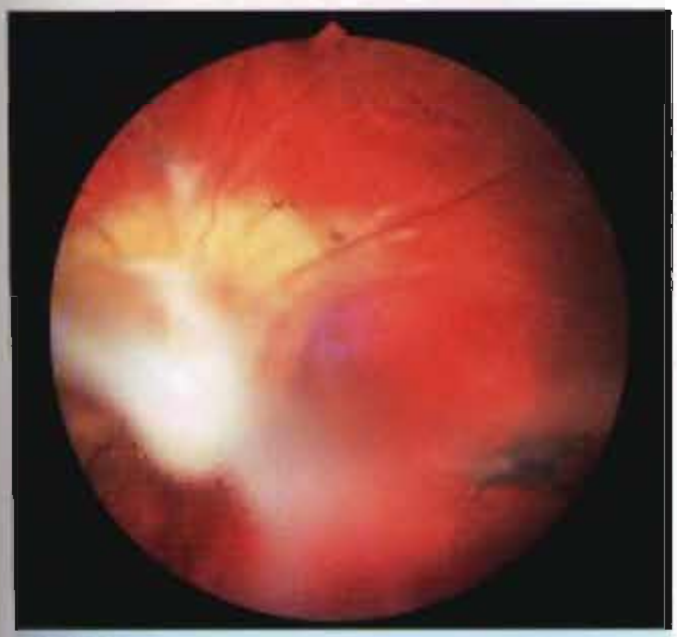


Fig. 10.78
Tractional retinal detachment due to a toxocara granuloma

Fig. 10.79
Peripheral toxocara granuloma

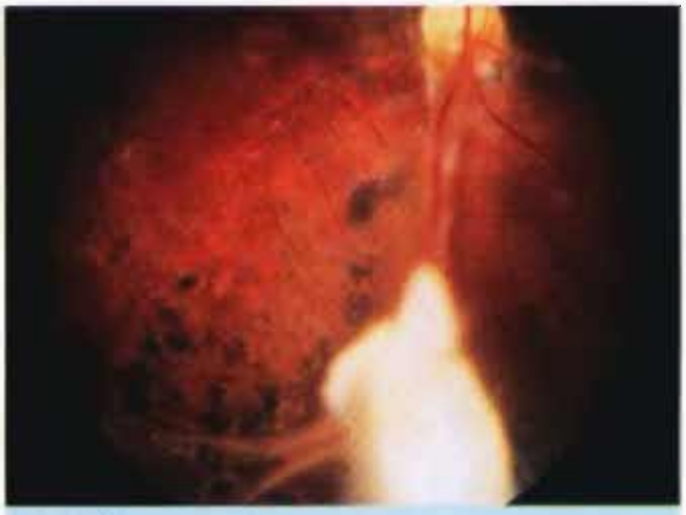


Fig. 10.80
Peripheral toxocara granuloma with vitreous bands (Courtesy of K. Rahman)

Diagnostic tests

1. **ELISA** can be used to determine the level of serum antibodies to *Toxocara canis*. When ocular toxocariasis is suspected, exact ELISA titres should be requested, including testing of undiluted serum. Any positive titre is consistent with, but not necessarily diagnostic of, toxocariasis. It must therefore be interpreted in conjunction with the clinical findings. A positive titre does not therefore exclude the possibility of retinoblastoma.
2. **Ultrasonography** may be useful both in establishing the diagnosis in eyes with hazy media and in excluding other causes of leukocoria. Pseudocystic transformation of the peripheral vitreous appears to be a specific feature of peripheral granulomas.

Choroidal pneumocystosis

Pneumocystis carinii, an opportunistic protozoan parasite, is a major cause of morbidity and mortality in AIDS. Choroidal involvement is an important sign of extrapulmonary dissemination. Most patients with choroiditis have received inhaled aerosolized pentamidine as prophylaxis against *Pneumocystis carinii* pneumonia. This, however, only protects

Fig. 10.81
Choroidal pneumocystosis (Courtesy of S. Mitchell)

the lungs and does not prevent the organisms from disseminating throughout the body. Choroiditis implies a grave prognosis for life.

1. **Signs.** Variable number of flat, yellow, round, choroidal lesions which are frequently bilateral (Fig. 10.81). The vitreous is uninvolved and visual acuity usually unimpaired, even in sub-foveal involvement.
2. **Treatment** with intravenous co-trimoxazole (trimethoprim–sulphamethoxazole) or pentamidine effects resolution within several weeks.

Fungal uveitis

Histoplasmosis

Histoplasmosis is a fungal infection caused by *Histoplasma capsulatum*. Ocular histoplasmosis is asymptomatic unless it causes maculopathy. The vitreous remains clear and is never involved.

Asymptomatic lesions

1. **Atrophic 'histo spots'** are small, roundish, slightly irregular, yellowish-white lesions, scattered throughout the mid-retinal periphery (Fig. 10.82) and posterior pole, which may be associated with small pigment clumps.
2. **Focal peripapillary atrophic** lesions, which are less common, are irregular and punched out, resembling the peripheral spots (Fig. 10.83).
3. **Diffuse parapapillary atrophy** extending up to half a disc diameter beyond the disc margin (Fig. 10.84).
4. **Linear peripheral streaks** of chorioretinal atrophy (Fig. 10.85).

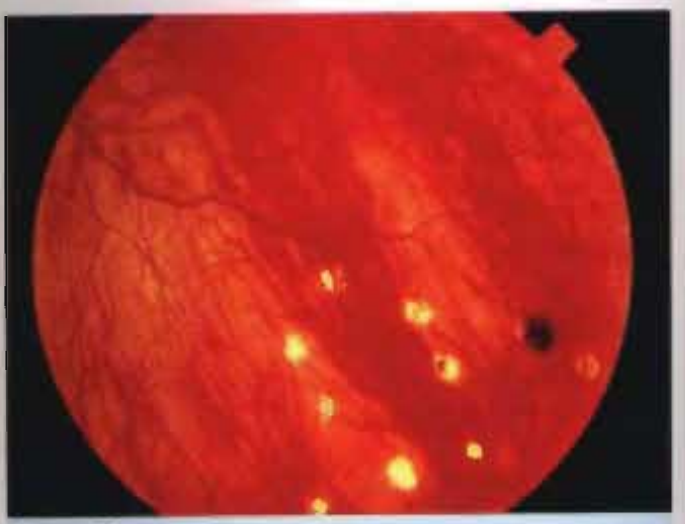


Fig. 10.82
Peripheral 'histo spots'

Fig. 10.83
Focal peripapillary atrophic spots in histoplasmosis

Fig. 10.84
Diffuse parapapillary atrophy and peripheral atrophic spots in histoplasmosis

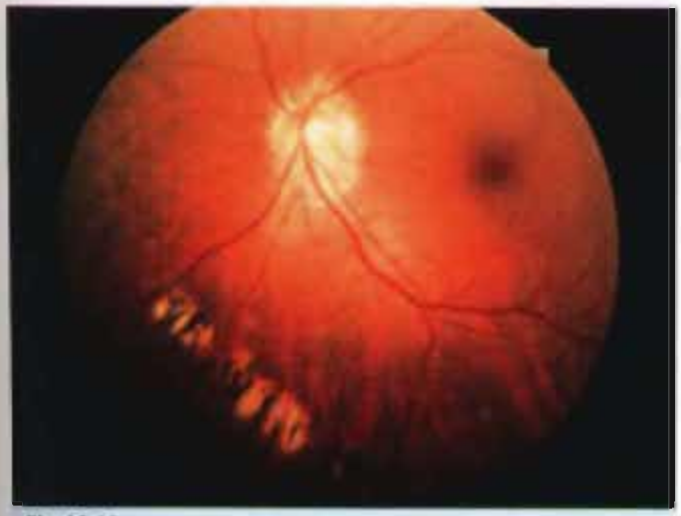


Fig. 10.85
Peripheral linear atrophic streaks in histoplasmosis

Exudative maculopathy

Choroidal neovascularization (CNV) is a late manifestation which usually develops between the ages of 20 and 45 years in about 5% of eyes. In most cases, it is associated with an old macular 'histo spot', although occasionally it may develop within a parapapillary lesion. Very rarely, CNV may occur in the absence of a pre-existing scar.

1. **The clinical course** of maculopathy is variable.
   - The CNV may initially leak fluid and give rise to metamorphopsia, blurring of central vision and a scotoma. Slit-lamp biomicroscopy shows macular elevation by serous fluid and an underlying focal yellow-white or grey lesion. In 12% of eyes the subretinal fluid absorbs spontaneously and visual symptoms regress.
   - A dark green-black ring frequently develops on the surface of the yellow-white lesion which bleeds into the subsensory retinal space, causing a marked drop in visual acuity. Rarely the haemorrhage resolves and visual acuity improves.
   - In some eyes, the initial CNV remains active for about 2 years, giving rise to repeated haemorrhages. This finally causes profound and permanent impairment of central vision resulting from the development of a fibrous disciform scar at the fovea.

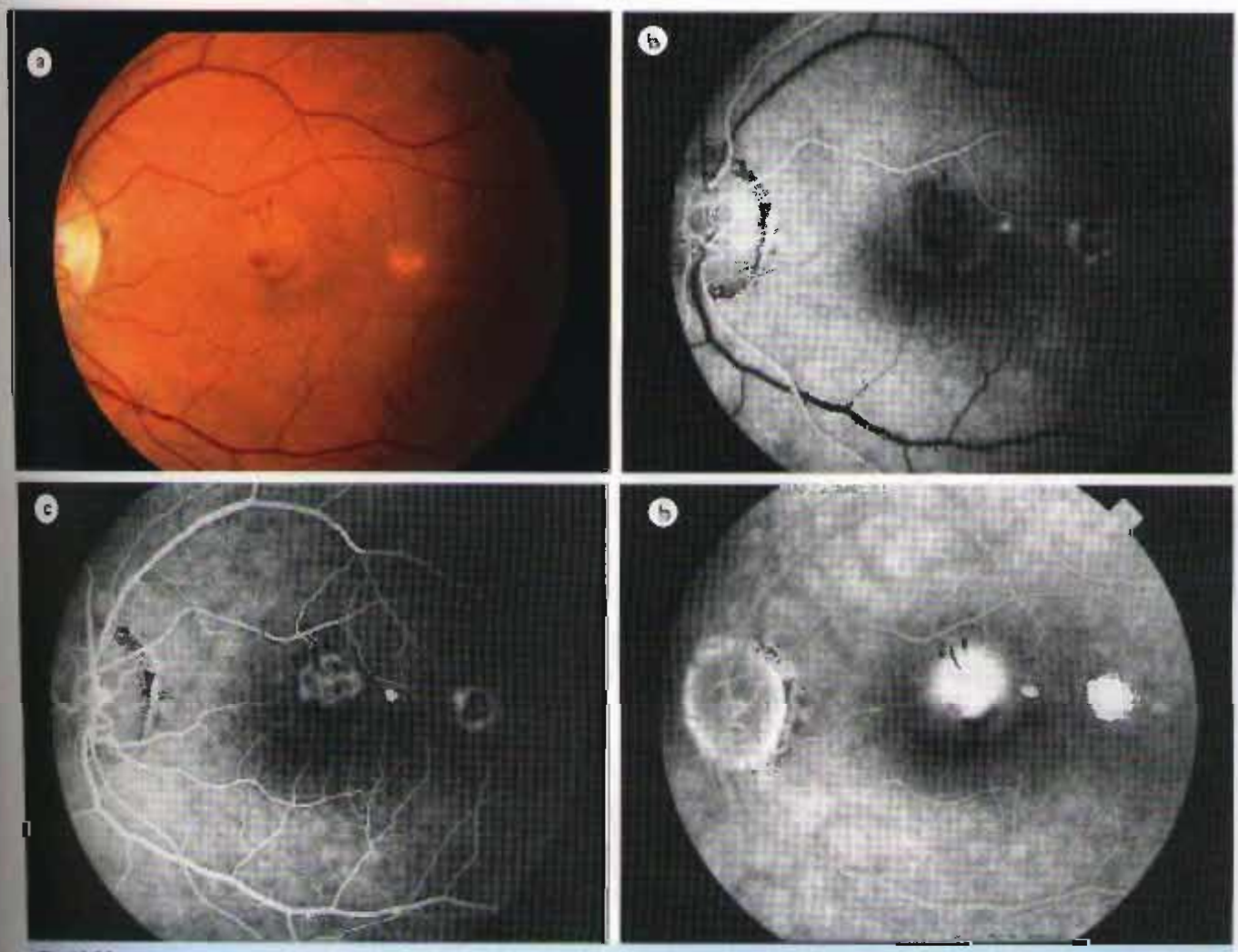


Fig. 10.86
Choroidal neovascularization in histoplasmosis (see text). **(a)** Foveal oedema and haemorrhage; **(b–d)** FA showing juxtafoveal choroidal neovascularization. A 'histo-spot' temporal to the fovea is also present. (Courtesy of S. Milewski)

2. **Monitoring** is important because patients with CNV in one eye and an asymptomatic atrophic macular scar in the other are likely to develop exudative maculopathy in the second eye. They should therefore test themselves daily with an Amsler grid to detect early metamorphopsia because without treatment 60% of eyes with CNV have a final visual acuity of less than 6/60.
3. **Treatment** by laser photocoagulation is currently the treatment of choice of extrafoveal CNV. Pre-treatment fluorescein angiography (FA) is vital in evaluating location and extent of CNV (Fig. 10.86). Surgical removal of subfoveal CNV may be indicated in selected cases. Photodynamic therapy of subfoveal lesions also shows promise.

Candidiasis

Candida albicans, a yeast, is a common commensal of the human skin, mouth, gastrointestinal tract and vagina, with a propensity towards opportunistic infection. Candidaemia, which may result in ocular involvement, occurs in three main groups: (a) *intravenous drug addicts*, (b) *patients with long-term indwelling catheters* and (c) *immunocompromised patients*.

Clinical features

1. **Presentation** is with gradual unilateral blurring of vision and floaters.
2. **Signs** (in chronological order)
   - Focal or multifocal choroiditis (Fig. 10.87).
   - Multifocal retinitis manifests as small, round, white, slightly elevated lesions with indistinct borders (Fig. 10.88).
   - Enlargement of the retinal lesions and extension into the vitreous gel, giving rise to floating white 'cotton-ball' colonies (Fig. 10.89).

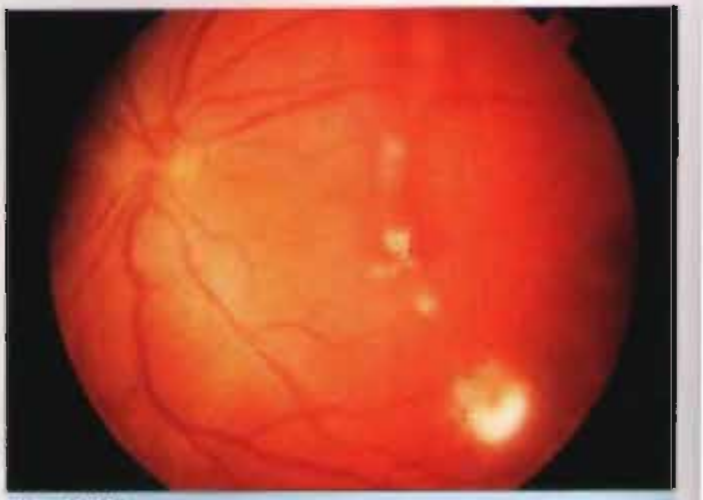


Fig. 10.88
Multifocal candida retinitis

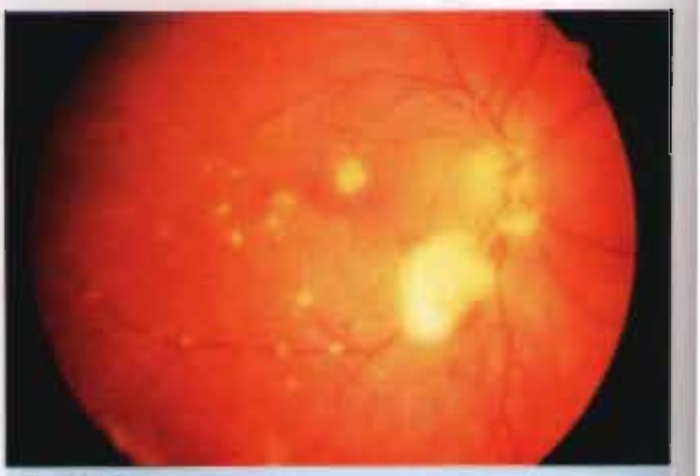


Fig. 10.89
Multifocal candida retinitis with vitreous 'cotton balls' (Courtesy of J. Salmon)

Fig. 10.87
Focal candida choroiditis

Fig. 10.90
Candida endophthalmitis

- Chronic endophthalmitis characterized by severe vitreous infiltration (Fig. 10.90).
- Retinal necrosis and retinal detachment.

3. **Investigations** involving vitreous cultures and PCR may be required to confirm the diagnosis.

Treatment

1. **Medical treatment** involves a combination of oral 5-fluorocytosine (flucytosine) 150 mg/kg daily and ketoconazole 200–400 mg daily for 3 weeks. Alternative therapy in resistant cases is intravenous amphotericin in 5% dextrose, given over a period of several days until a cumulative dose of 200 mg is reached. The initial daily dose is 5 mg and after a few days this can be increased to 20 mg.
2. **Pars plana vitrectomy** is indicated for endophthalmitis. At vitrectomy, smears and cultures should be taken to confirm the diagnosis and test sensitivity to antifungal agents. Intravitreal injection of 5 μg of amphotericin is also administered.

Cryptococcal choroiditis

Cryptococcus neoformans frequently infects the central nervous system in patients with AIDS, although clinical ocular involvement is rare. When it does occur, it usually follows systemic disease, most commonly cryptococcal meningitis.

1. **Signs** (in chronological order)
   - Multifocal, yellow-white, choroidal lesions which are usually asymptomatic (Fig. 10.91).
   - Retinal involvement characterized by small, glistening spheres at the vitreoretinal interface is rare.
   - Optic nerve involvement may result in rapid visual loss.
2. **Treatment** of sight-threatening lesions is with intravenous amphotericin. Endophthalmitis may require vitrectomy and intravitreal amphotericin.

Mycobacterial uveitis

Tuberculosis

Tuberculosis (TB) is a chronic granulomatous infection caused by bovine (*Mycobacterium bovis*) or human tubercle bacilli (*Mycobacterium tuberculosis*). The former is acquired by drinking milk from infected cattle and the latter by 'droplet infection' (*see* Chapter 20). Tuberculous uveitis is rare in the developed world. However, it may occur without systemic signs of TB, rendering definitive diagnosis difficult. The diagnosis of tuberculous uveitis is therefore often presumptive, based on indirect evidence, such as intractable uveitis unresponsive to steroid therapy and negative findings for other causes of uveitis.

1. **Clinical features**
   a. ***Chronic iridocyclitis***, usually granulomatous, but occasionally non-granulomatous, is the most frequent feature.
   b. ***Choroiditis*** may be local or multifocal. Rarely, a large solitary choroidal granuloma (Fig. 10.92) may be mistaken for a choroidal tumour.
   c. ***Periphlebitis*** may lead to peripheral retinal capillary closure and neovascularization.
   d. ***Panuveitis.***
2. **Treatment** is with antituberculous drugs.

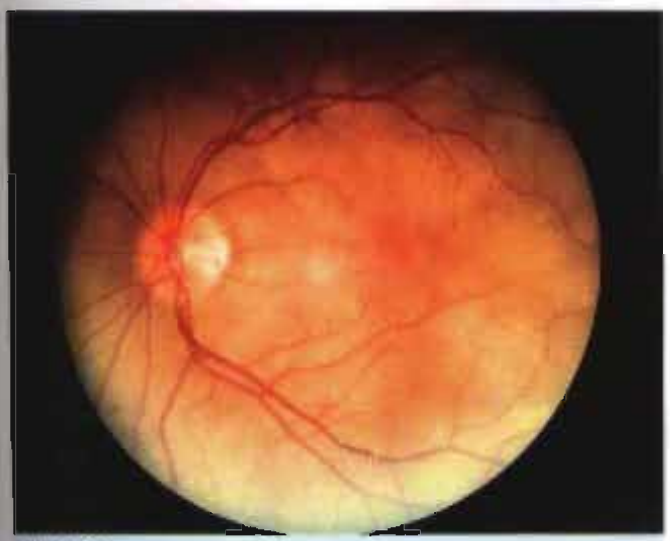


Fig. 10.91
Cryptococcal choroiditis (Courtesy of S. Mitchell)

Fig. 10.92
Solitary choroidal tuberculous granuloma

Leprosy

Leprosy (Hansen disease) has the highest incidence of ocular complications of any systemic disease. The pathogenic agent, *Mycobacterium leprae*, has an affinity for skin, peripheral nerves and the anterior segment of the eye. Leprosy may be (a) *lepromatous* or (b) *tuberculoid* (*see* Chapter 20). Uveitis is more common in the former.

1. **Acute iritis** is thought to be caused by immune complex deposition in the uvea. It may be associated with systemic symptoms such as fever and swelling of skin lesions. Intraocular inflammation may be precipitated by initiation or withdrawal of systemic antileprosatous therapy. Treatment is with topical steroids.
2. **Chronic iritis** is the result of direct invasion by bacilli. It is more resistant to conventional therapy than the acute type, because it may not be a true uveitis but a neuroparalytic inflammation caused by involvement of the iris nerves.
   - A pathognomonic sign of lepromatous leprosy is the presence at the pupillary margin of small, glistening 'iris pearls' resembling a necklace (Fig. 10.93a).
   - The 'pearls' slowly enlarge and coalesce, become pedunculated and drop into the anterior chamber, from which they eventually disappear (Fig. 10.93b).
   - Eventually, the iris becomes atrophic and the pupil miosed (Fig. 10.94).
3. **Other manifestations** include madarosis, trichiasis, conjunctivitis, episcleritis, keratitis and scleritis (Fig. 10.95a). Facial paralysis and anaesthesia, often bilateral, may occur, secondary to involvement of the facial and trigeminal nerves. Keratitis is due to a combination of trichiasis, lagophthalmos (Fig. 10.95b), corneal anaesthesia and secondary infection.

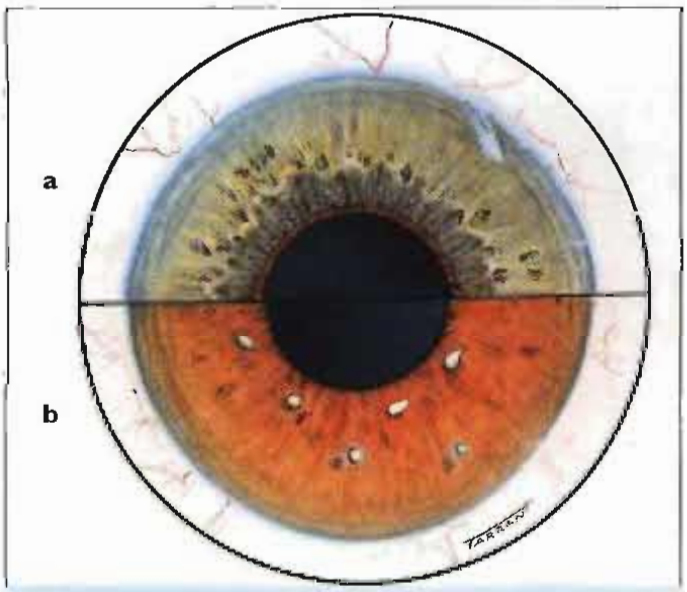


Fig. 10.93
Chronic lepromatous iritis. (a) Small iris 'pearls'; (b) large iris 'pearls' which have dropped into the anterior chamber

Fig. 10.94
Severe miosis and iris atrophy in chronic lepromatous iritis
(Courtesy of T. ffytche)

Fig. 10.95
Leprosy. (a) Severe corneal scarring; (b) lagophthalmos
(Courtesy of T. ffytche)

Spirochaetal uveitis

Acquired syphilis

Acquired syphilis is a sexually transmitted infection caused by *Treponema pallidum*. It is a systemic disease which, when untreated, has overt and covert stages (*see* Chapter 20).

Clinical features

Ocular syphilis is uncommon and there are no pathognomonic signs. Eye involvement typically occurs during the secondary and tertiary stages although occasionally it may be seen during primary syphilis. The disease must therefore be suspected in any case of intraocular inflammation resistant to conventional therapy.

1. **External features** include madarosis, scleritis and keratitis.
2. **Iridocyclitis** occurs in about 4% of patients with secondary syphilis and is bilateral in 50%.
   - The inflammation is usually acute and unless appropriately treated becomes chronic.
   - In some cases, iridocyclitis is first associated with dilated iris capillaries (roseolae) (Fig. 10.96), which may develop into more localized papules and subsequently into larger yellowish nodules.
   - Various types of post-inflammatory iris atrophy may ensue.
3. **Multifocal chorioretinitis** is the next most common finding.
   - Multiple foci of choroiditis later evolve into healed lesions, which appear as focal areas of chorioretinal atrophy associated with hyperpigmentation (Fig. 10.97).
   - Occasionally extensive pigmentary changes with perivascular bone spicules, similar to those seen in retinitis pigmentosa, may be associated with night blindness and a ring scotoma.

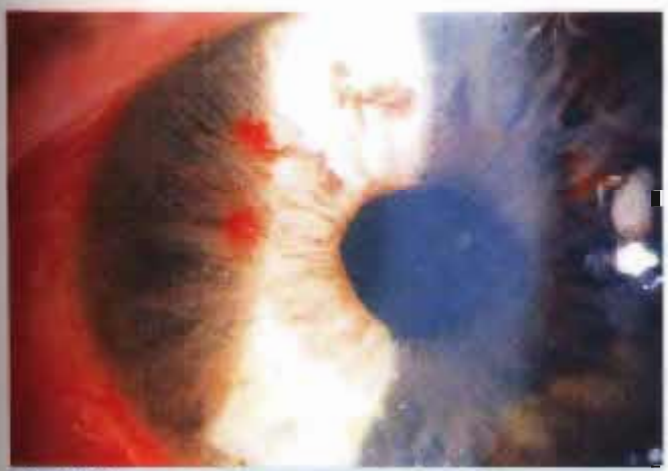


Fig. 10.96
Dilated iris capillaries

Fig. 10.97
Old multifocal syphilitic choroiditis (Courtesy of J. Salmon)

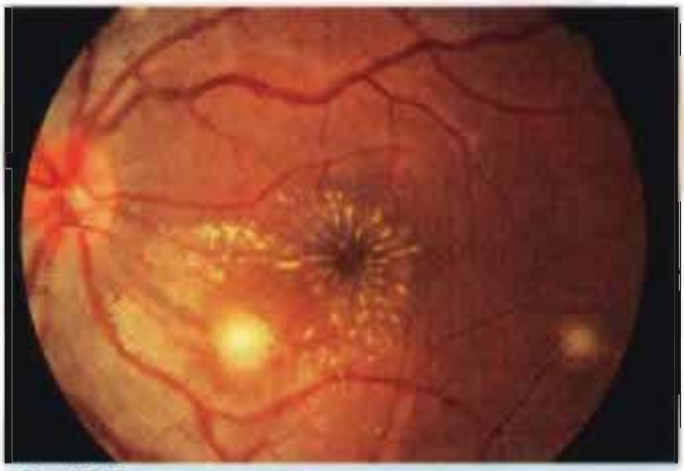


Fig. 10.98
Active syphilitic neuroretinitis (Courtesy of J. Salmon)

4. **Focal chorioretinitis** is less common and frequently bilateral. It is characterized by an inflammatory focus near the disc or at the macula.
5. **Neuroretinitis** primarily involves the retina and optic nerve head independently of choroidal inflammation.
   - The fundus shows disc oedema, engorged veins and a macular star (Fig. 10.98).
   - Cotton wool spots or flame-shaped haemorrhages may appear.
   - Unless treated, the retinal blood vessels eventually become replaced by white strands and optic atrophy ensues (Fig. 10.99).
6. **Neuro-ophthalmological** features include pupillary abnormalities, optic neuropathy, ocular motor nerve palsies and visual field defects.

Treatment

Conventional doses of penicillin are inadequate; the therapeutic regimen is the same as for neurosyphilis (which should be ruled out by lumbar puncture). One of the following regimens may be used:

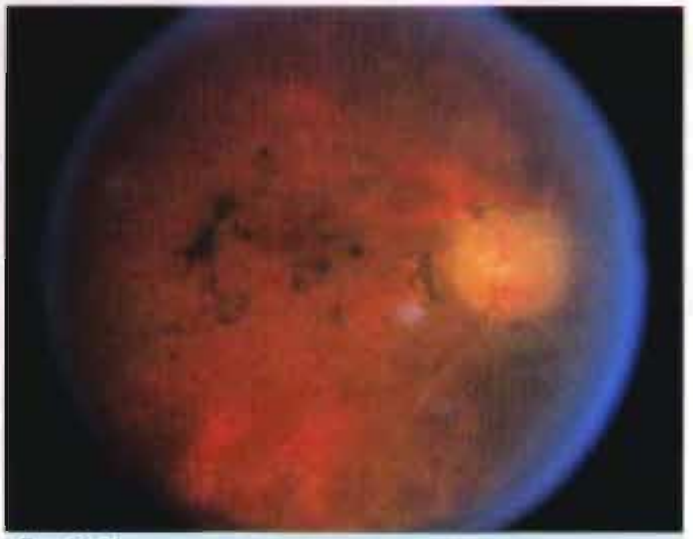


Fig. 10.99
End-stage syphilitic neuroretinitis with vascular attenuation and consecutive optic atrophy

- Intravenous aqueous penicillin G 12–24 mega units (MU) daily for 10–15 days.
- Intramuscular procaine penicillin 2.4 MU daily, supplemented with oral probenecid (2 g daily), for 10–15 days.
- Oral amoxycillin 3 g b.d. for 28 days.
- Penicillin-allergic patients can be treated with oral tetracycline or erythromycin 500 mg q.i.d. for 30 days.

Lyme disease

Lyme disease is caused by *Borrelia burgdorferi*, which is similar to the treponeme that causes syphilis. It is transmitted through the bite of its vector, the deer tick *Ixodes* sp. As with syphilis, both early and late manifestations develop in many organ systems (*see* Chapter 20).

1. **Uveitis** may take the form of granulomatous iridocyclitis, intermediate uveitis, retinal vasculitis and occasionally peripheral multifocal choroiditis.
2. **Neuro-ophthalmological features** include optic neuritis, neuroretinitis and ocular motor nerve palsies.
3. **Other features** include periorbital oedema, conjunctivitis, episcleritis, keratitis and orbital myositis.
4. **Treatment** is with doxycycline 100 mg b.d. for 2–3 weeks.

Common specific uveitis entities

Fuchs uveitis syndrome

Fuchs uveitis syndrome (FUS) or Fuchs heterochromic cyclitis is a chronic, non-granulomatous, anterior uveitis of insidious onset. It typically affects one eye of a young adult,

Fig. 10.100
Heterochromia iridis and cataract in left Fuchs uveitis syndrome

although it can also occur during childhood and may rarely be bilateral. Although FUS accounts for about 4% of all cases of uveitis, it is frequently misdiagnosed and overtreated. The heterochromia (difference in iris colour) may be absent or difficult to detect, particularly in brown-eyed individuals, unless the patient is examined in daylight with undilated pupils.

Presentation

- Gradual blurring of vision secondary to cataract formation is the most common.
- Chronic annoying floaters.
- Colour difference between the two eyes (Fig. 10.100).
- Incidental detection.

General signs

1. **Keratic precipitates** (KP) are characteristic and possibly pathognomonic. They are small, round or stellate, grey-white in colour and scattered throughout the corneal endothelium (Fig. 10.101). They may come and go but never become confluent or pigmented. Feathery fibrin filaments may be seen in between the KP.

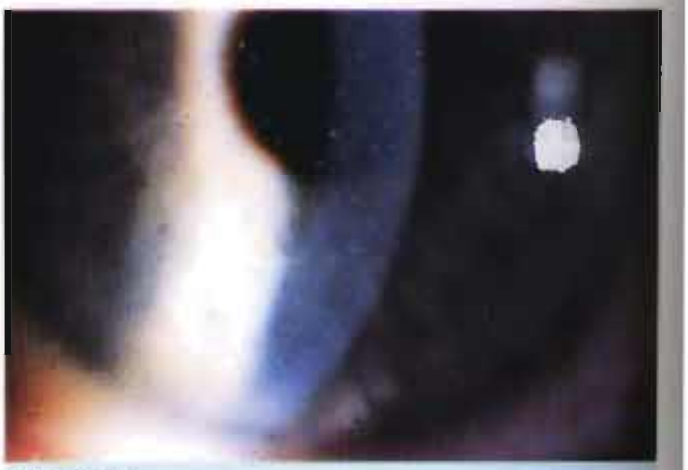


Fig. 10.101
Keratic precipitates in Fuchs uveitis syndrome

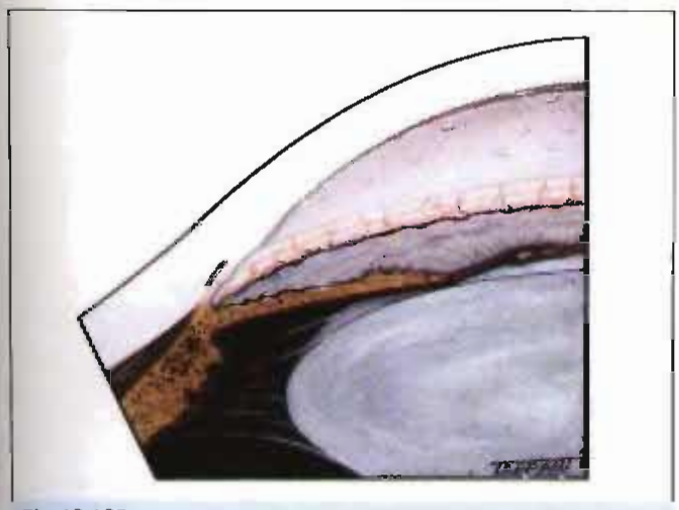


Fig. 10.102
New vessels in the angle in Fuchs uveitis syndrome

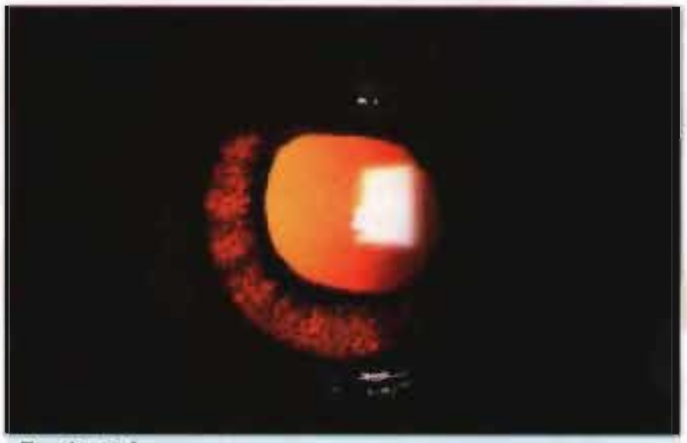


Fig. 10.104
Transillumination defects due to iris atrophy in Fuchs uveitis syndrome

2. **Aqueous humour** shows a faint flare and never more than +2 cells.
3. **Vitritis** and stringy opacities are common and may be the presenting symptom.
4. **Gonioscopy** may be normal or may show one of the following:
   - Fine radial twig-like vessels in the angle (Fig. 10.102) are common and are probably responsible for the filiform haemorrhages which develop on anterior chamber paracentesis opposite the puncture site (Amsler sign).
   - A membrane obscuring angle details.
   - Small, non-confluent, irregular, peripheral anterior synechiae.

Iris signs

1. **Posterior synechiae do not occur**, except after cataract surgery.
2. **Diffuse stromal iris atrophy**
   - The earliest finding is loss of iris crypts.
   - Advanced stromal atrophy makes the affected iris appear dull with loss of detail, giving rise to a washed-out appearance, particularly in the pupillary zone (Fig. 10.103).
   - The normal radial iris blood vessels appear prominent due to lack of stromal support.
3. **Posterior pigment layer iris atrophy** is patchy and best detected by retroillumination (Fig. 10.104).
4. **Iris nodules** may be present.
5. **Rubeosis iridis** consisting of fine, irregular, fragile, neovascularization on the iris surface is fairly common.
6. **Mydriasis** resulting from atrophy of the pupillary sphincter may be present.
7. **Iris crystals** occur in a minority of cases.
8. **Heterochromia iridis** is an important and common sign.
   - Most frequently the affected eye is hypochromic (Fig. 10.105) although in about 10% it is hyperchromic.
   - In a small proportion of cases, the heterochromia is congenital.
   - The nature of heterochromia is determined by the relative degrees of atrophy of the stroma and posterior pigment epithelium, as well as the patient's natural iris colour.

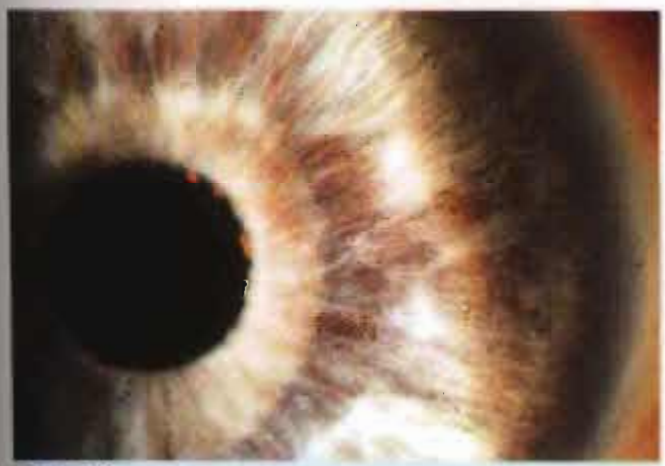


Fig. 10.103
Stromal iris atrophy in Fuchs uveitis syndrome

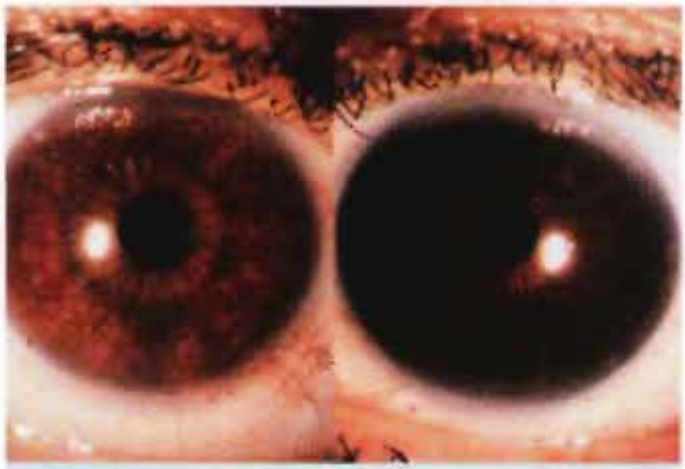


Fig. 10.105
Heterochromia iridis in right Fuchs uveitis syndrome

- Predominantly stromal atrophy allows the posterior pigmented layer to show through and become the dominant pigmentation, so that the eye becomes hyperchromic.
- In general, a brown iris becomes less brown and a blue iris assumes a more saturated blue colour.

Complications

FUS runs a chronic course lasting many years. The two main complications are cataract and glaucoma, both of which may be enhanced by the inadvertent use of topical steroids.

1. **Cataract** is extremely common and does not differ from that associated with other types of anterior uveitis. The results of surgery with posterior chamber intraocular lens implantation are good, although the operation may be complicated by hyphaema.
2. **Glaucoma** is the most serious threat to vision and is frequent when the follow-up period is long (*see* Chapter 9).

Treatment

1. **Topical steroids** are ineffective.
2. **Mydriatics** are unnecessary because posterior synechiae do not occur.
3. **Posterior sub-Tenon** injections of a long-acting preparation such as triamcinolone acetonide may be beneficial for troublesome vitreous floaters although improvement is usually temporary.
4. **Vitrectomy** may be considered for severe vitreous opacification, unresponsive to periocular steroid injections.

Differential diagnosis of heterochromia iridis

Apart from FUS, the following conditions may give rise to heterochromia:

1. **Hypochromia**
   - Congenital.
   - Horner syndrome, particularly if congenital.
2. **Hyperchromia**
   - Oculodermal melanocytosis (naevus of Ota).
   - Ocular siderosis.
   - Diffuse iris naevus or melanoma.
   - Unilateral use of topical latanoprost.
   - Sturge–Weber syndrome (rare).

Intermediate uveitis

Intermediate uveitis is an idiopathic, insidious, inflammatory disease affecting the pars plana, peripheral retina and underlying choroid. It accounts for about 8% of all cases of uveitis. Although often bilateral, involvement is frequently asymmetrical. On long-term follow-up 10–15% of patients subsequently develop multiple sclerosis, a common immunogenetic predisposition appearing to be HLA-DR15.

Clinical features

1. **Presentation** is in the second to fourth decades with increasing floaters, or less commonly with impairment of central vision secondary to macular oedema.
2. **Signs**
   *a. **Vitritis*** is predominant although the anterior chambers may display mild activity. The severity of vitritis may vary.
   - Cells in the anterior vitreous (Fig. 10.106).
   - Gelatinous exudates ('snowballs' or 'cotton balls') (Fig. 10.107).
   - Sheet-like condensations in long-standing cases (Fig. 10.108).
   - Rarely the entire vitreous may become opaque (Fig. 10.109).

   *b. **Peripheral retinal periphlebitis*** is common and usually mild.

   *c. **Snowbanking*** is the hallmark of pars planitis, which is a subset of intermediate uveitis. It consists of a grey-white plaque involving the inferior pars plana, visible

Fig. 10.106
Anterior vitreous cells in intermediate uveitis

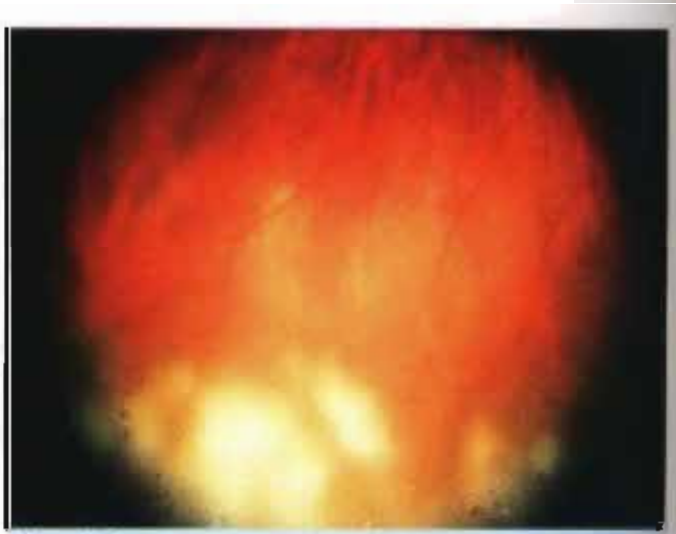


Fig. 10.107
Vitreous 'cotton balls' in intermediate uveitis

Fig. 10.108
Vitreous condensations in long-standing intermediate uveitis

Fig. 10.109
Severe vitreous opacification in intermediate uveitis

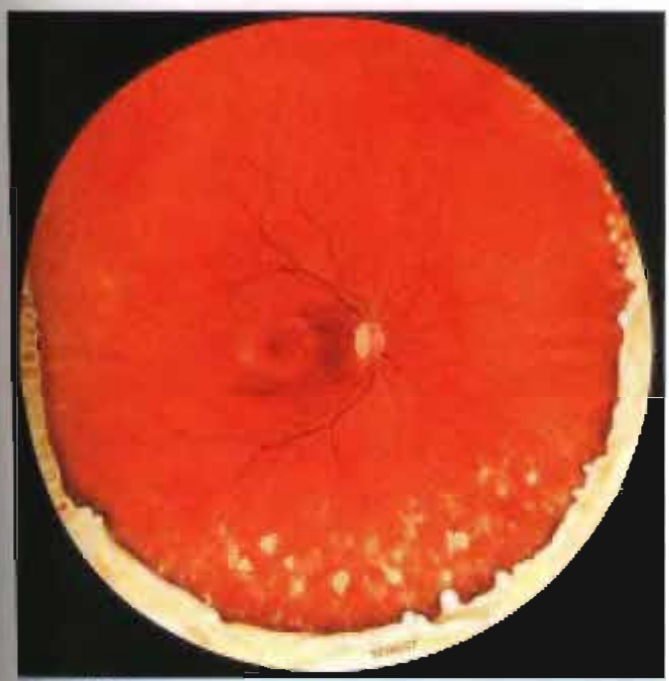


Fig. 10.110
Inferior 'snowbanking' in pars planitis

only on indirect ophthalmoscopy with scleral indentation (Fig. 10.110). In advanced cases the plaque may extend posteriorly to cover the peripheral retina.

3. **Course**. Some patients have a single, mild, self-limiting episode lasting a few months but most have chronic smouldering inflammation lasting several years, with multiple subacute exacerbations and incomplete remissions. Despite this, the prognosis is relatively good.

Complications

1. **Cystoid macular oedema** is the most common cause of visual impairment.
2. **Macular epiretinal gliosis** is also frequent.
3. **Secondary cataract** develops more frequently in eyes with severe and prolonged inflammation.
4. **Tractional retinal detachment** may occur in advanced cases as a result of contraction of fibrovascular tissue at the pars plana (which may also result in vitreous haemorrhage).
5. **Cyclitic membrane formation** is the result of massive proliferation of vascularized exudate on to and behind the posterior lens capsule. Traction by the membrane on the ciliary body may cause ciliary detachment, with diminished secretion of aqueous, resulting in ocular hypotony and eventual phthisis bulbi.

Treatment

It is important not to over-treat this condition. The main indication for treatment is a visual acuity of 6/12 or less secondary to persistent cystoid macular oedema.

1. **Posterior sub-Tenon injections** of triamcinolone acetonide (Kenalog) or methylprednisolone acetate (Depomedrone) are effective in most cases. The necessity for repeated injections is governed by visual acuity rather than severity of vitritis.
2. **Systemic** steroids or immunosuppressive agents may be required if resistant to periocular steroids.
3. **Cryotherapy** to the vitreous base may be beneficial in controlling inflammation and active neovascularization.
4. **Pars plana vitrectomy** may be required for severe and persistent complications such as vitreous haemorrhage, dense vitreous opacification, epiretinal membranes and tractional retinal detachment.

Differential diagnosis

The following conditions may also be characterized by vitreous inflammation in the absence of significant retinal findings:

1. **Fuchs uveitis syndrome**
   - Similarities: may affect young individuals and present with floaters and mild anterior uveitis.
   - Differences: unilateral and subtle iris atrophy is present in the majority of cases.
2. **Systemic diseases** which may be associated with 'secondary intermediate uveitis' include sarcoidosis, Lyme

disease, non-Hodgkin B-cell lymphoma, cat-scratch fever and Whipple disease.

Juvenile chronic iridocyclitis

While juvenile idiopathic arthritis is the most common systemic association of chronic iridocyclitis in children, many patients with juvenile chronic iridocyclitis are otherwise healthy. The majority of patients are also girls. As the onset of intraocular inflammation is frequently insidious and asymptomatic, most cases are not diagnosed until visual acuity is reduced from complicated cataract or the parents notice a white patch on the cornea caused by band keratopathy (Fig. 10.111). In a small number of cases the uveitis is detected by chance.

Acute anterior uveitis in young adults

While ankylosing spondylitis is the most common systemic association of acute anterior uveitis (Fig. 10.112), many patients have no underlying systemic disease, although about 45% carry HLA-B27. The risk to HLA-B27 negative patients (particularly females) of subsequently developing ankylosing spondylitis is very small, although some HLA-B27 positive patients (particularly males) will subsequently develop the disease.

Fig. 10.111
Band keratopathy in juvenile chronic iridocyclitis

Fig. 10.112
Acute anterior uveitis with hypopyon in ankylosing spondylitis

Idiopathic multifocal white dot syndromes

Acute multifocal posterior placoid pigment epitheliopathy

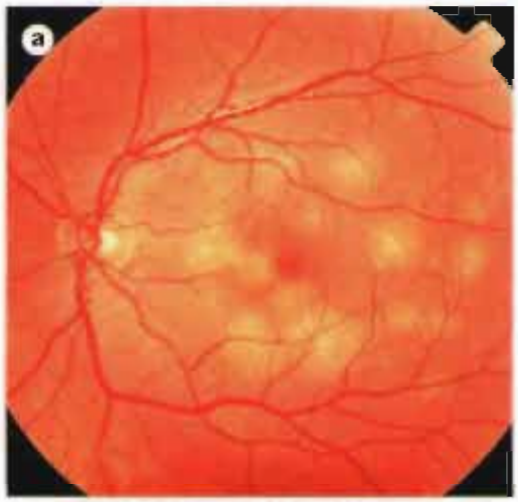
Acute multifocal posterior placoid pigment epitheliopathy (AMPPPE) is an uncommon, idiopathic, bilateral, self-limiting condition which is frequently associated with HLA-B7 and HLA-DR2. Although there is no treatment the prognosis is good.

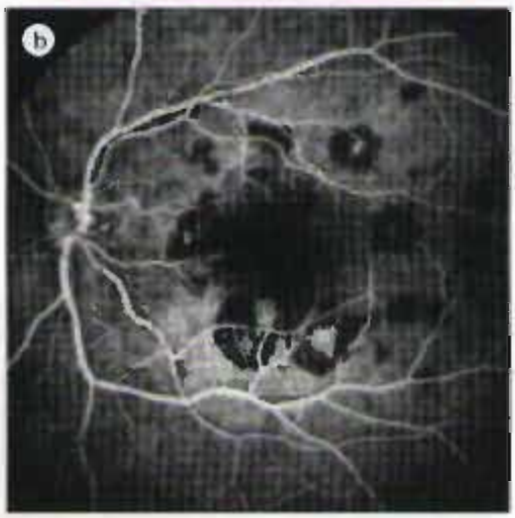
1. **Presentation** is in the third to fifth decades with subacute unilateral visual impairment which becomes bilateral within a few days. About a third of patients have a preceding 'flu-like' illness which may be associated with erythema nodosum.
2. **Signs**
   - Multiple, large, cream or greyish-white, subretinal, plaque-like lesions of variable size which begin at the posterior pole and then extend to the post-equatorial fundus (Fig. 10.113a).
   - Associated findings include anterior uveitis, mild vitritis, disc oedema and retinal periphlebitis.
3. **FA** of active lesions shows early dense hypofluorescence due to blockage of choroidal fluorescence (Fig. 10.113b). The late phase shows hyperfluorescence due to staining (Fig. 10.113c). These findings can be explained on the basis of occlusion of the choriocapillaris which leads to swelling of the retinal pigment epithelium (RPE).
4. **Course.** After a few weeks the fundus lesions gradually subside and within a few months visual acuity returns to normal or near normal. Variable residual signs consist of multifocal areas of RPE depigmentation and clumping (Fig. 10.114). Some patients complain of residual para-central visual field defects and a few develop late CNV.

Serpiginous choroidopathy

Serpiginous choroidopathy is an uncommon, idiopathic, bilateral, progressive disease.

1. **Presentation** is in the fourth to sixth decades with unilateral blurring of vision or metamorphopsia. After a variable period of time the fellow eye is also affected although it is not uncommon to find evidence of inactive asymptomatic disease in the fellow eye at the time of presentation.





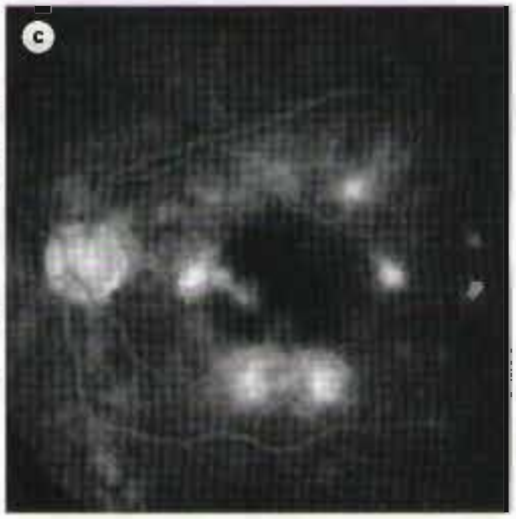


Fig. 10.113
Acute multifocal posterior placoid pigment epitheliopathy (see *text*) (Courtesy of S. Milewski)

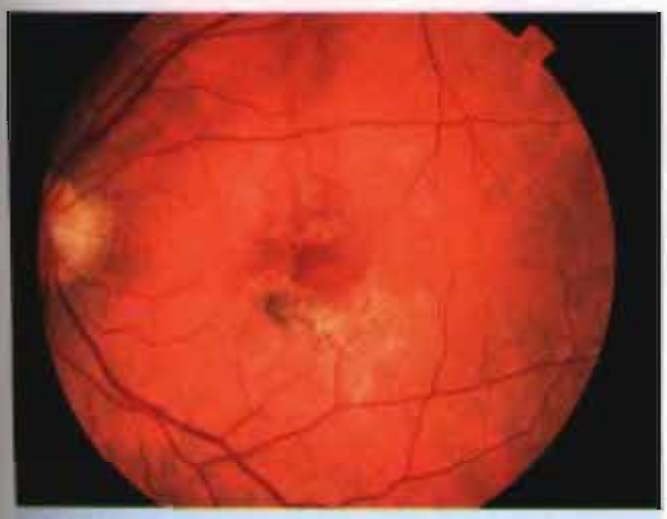


Fig. 10.114
Resolved acute multifocal posterior placoid pigment epitheliopathy

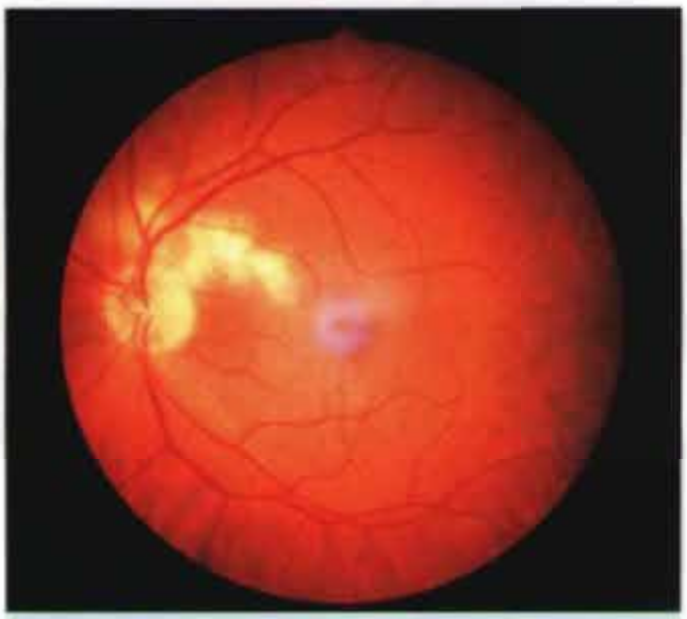


Fig. 10.115
Early serpiginous choroidopathy

2. Signs

- Active lesions are grey-white to yellow-white subretinal infiltrates with hazy borders, which later become lighter. They typically start around the optic disc (Fig. 10.115) and then gradually spread outwards in a snake-like manner and towards the macula (Fig. 10.116).

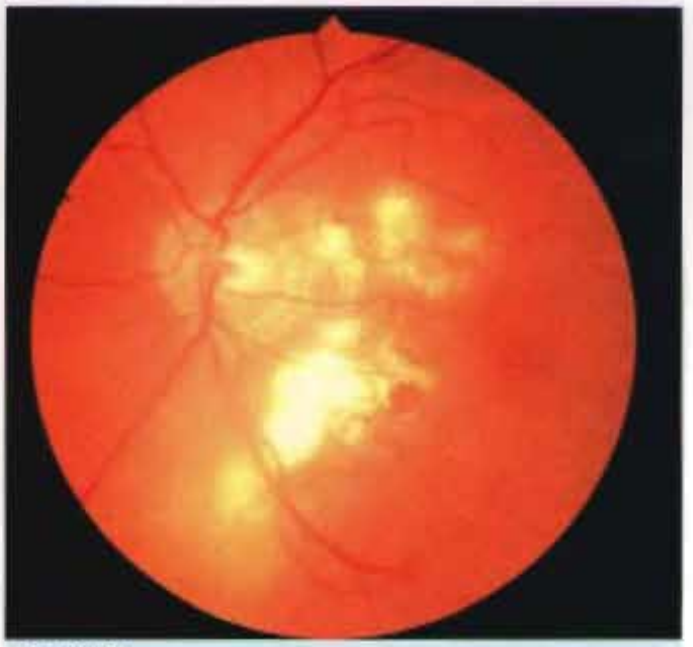


Fig. 10.116
More advanced serpiginous choroidopathy

Rarely the initial lesion involves the macula.

- Associated features include vitritis and mild anterior uveitis.

3. **FA** shows early hypofluorescence due to blockage and late hyperfluorescence due to staining.
4. **Electro-oculogram (EOG)** is subnormal.
5. **Course** is prolonged, lasting many years, in an episodic and recurrent fashion. Disease activity not uncommonly recurs after several months of remission. Recurrences are characterized by yellow-grey extensions of choroiditis (at the level of the choriocapillaris), contiguous with or as satellites to pre-existing areas of chorioretinal atrophy. Inactive lesions are characterized by scalloped, atrophic, 'punched-out' areas of choroidal atrophy associated with RPE changes. The long-term visual prognosis is poor, with permanent visual loss caused by foveal involvement occurring in about 50% of cases (Fig. 10.117). Some eyes develop CNV associated with an old scar which may be amenable to laser photocoagulation. Subretinal fibrosis is a rare late complication.
6. **Treatment** options include triple therapy with systemic steroids, azathioprine and cyclosporin although early monotherapy with cyclosporin may be adequate.

Fig. 10.117
Extensive involvement of the posterior pole in serpiginous choroidopathy

Birdshot retinochoroidopathy

Birdshot retinochoroidopathy is an uncommon, chronic, bilateral inflammatory disease, probably of autoimmune aetiology. About 90% of patients are positive for HLA-A29.

1. **Presentation** is in the sixth to seventh decades with blurring of vision, frequently associated with nyctalopia, disturbance of colour vision and floaters. The severity of visual disturbance is frequently out of proportion to the visual acuity, indicating diffuse retinal dysfunction.

Fig. 10.118
Birdshot retinochoroidopathy involving the macula and mid-periphery

2. **Signs**
   - Diffuse vitritis but minimal if any anterior uveitis.
   - Acute lesions consist of distinctive, subretinal, poorly defined, cream-coloured, small (100–300 μm) ovoid spots distributed in one of four patterns:
     a. Involving the macula and mid-periphery (Fig. 10.118, *see* Fig. 10.121a).
     b. With relative macular sparing (Fig. 10.119).
     c. With macular predominance.

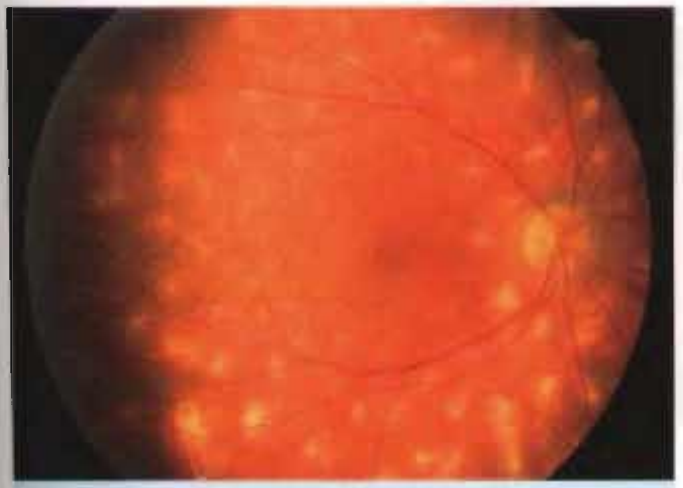


Fig. 10.119
Birdshot retinochoroidopathy with macular sparing

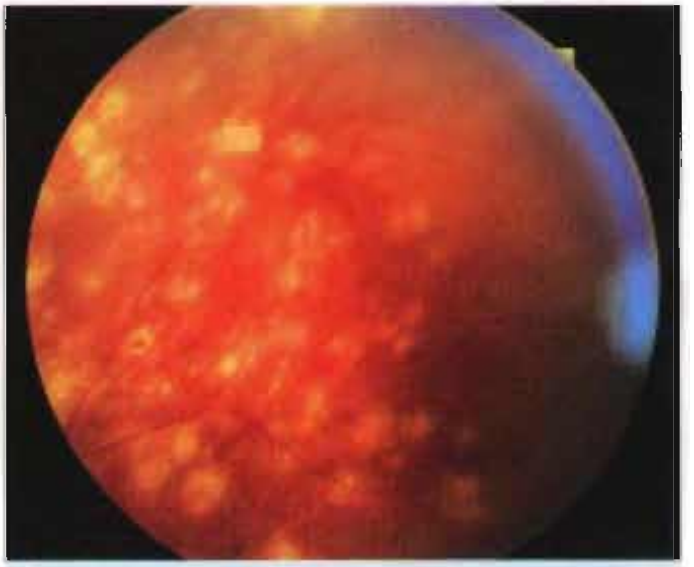
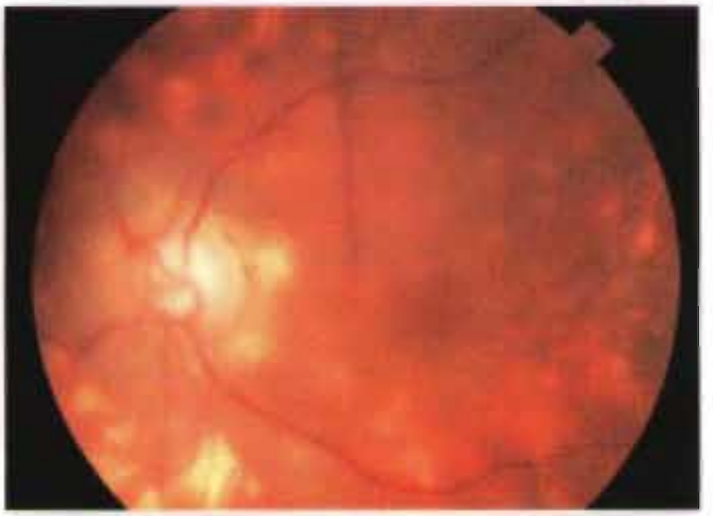


Fig. 10.120
Resolved birdshot retinochoroidopathy

d. Asymmetrical with inferonasal predominance of lesions and relative macular sparing.

- Over time the lesions may become confluent. Inactive lesions consist of well-delineated, white atrophic spots (Fig. 10.120).

3. **FA** of established active lesions shows disc staining and vascular leakage (Fig. 10.121b) but early birdshot lesions



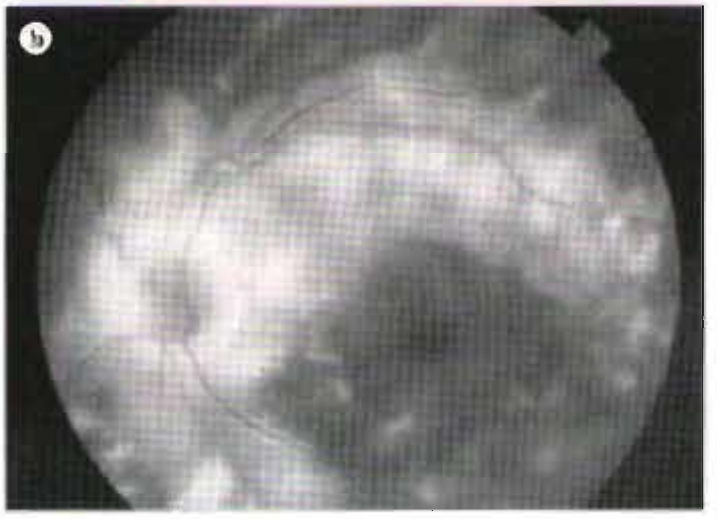


Fig. 10.121
Birdshot retinochoroidopathy (see *text*) (Courtesy of S. Milewski)

may remain silent throughout the angiogram, so that a greater number are seen clinically than angiographically.

4. **ICG** detects birdshot lesions more readily than FA. Typical findings in active disease are hypofluorescent dark spots during the intermediate phase of the angiogram which remain so, or become isofluorescent during the late phases. Two other features are indistinct choroidal vessels and late diffuse choroidal hyperfluorescence.
5. **Electroretinogram (ERG)** is subnormal.
6. **Course**. About 20% of patients have a self-limited course and maintain normal visual acuity. The remainder have a chronic course with exacerbations and remissions over several years with visual impairment due to CMO and occasionally epiretinal gliosis and CNV.
7. **Treatment**. Although currently there is no definitive treatment strategy the following may be considered:
   a. Steroids, both periocular or systemic, give inconsistent results.
   b. Cyclosporin, in uncontrolled studies, has been shown to be superior to steroid therapy and may prove to be the treatment of choice.

Fig. 10.123
Inactive punctate inner choriodopathy

Punctate inner choroidopathy

Punctate inner choroidopathy (PIC) is an uncommon, idiopathic, bilateral disease which typically affects myopic women.

1. **Presentation** is in the fourth to fifth decades with blurring of central vision, frequently associated with photopsia. In some cases photopsia may be present for several weeks prior to the development of clinical signs.
2. **Signs** (in chronological order)
   - Multiple, small, deep, yellow, indistinct spots involving the posterior pole, all at the same stage of evolution (Fig. 10.122). Plentiful lesions may be associated with serous sensory retinal elevation.
   - After a few weeks the acute lesions resolve, leaving behind sharply demarcated atrophic scars which may later enlarge and become pigmented (Fig. 10.123).
   - There is no intraocular inflammation.
3. **FA** shows hyperfluorescence of the lesions due to RPE window defects and, if present, CNV (Fig. 10.124b–d).
4. **ERG** is normal.
5. **Course**. After a variable period of time the fellow eye frequently becomes involved. Some patients develop foveal scarring or secondary CNV associated with a scar within a year of presentation. The prognosis is relatively good in patients without macular involvement.
6. **Treatment** is only possible for CNV with the following modalities:
   a. Laser photocoagulation.
   b. Systemic steroids may reduce subretinal vascular leakage and stabilize vision.
   c. Surgical excision of subfoveal CNV may be appropriate in selected cases.

Fig. 10.122
Active punctate inner choroidopathy (Courtesy of Moorfields Eye Hospital)

Multifocal choroiditis with panuveitis

Multifocal choroiditis with panuveitis is an uncommon, usually bilateral, recurrent inflammatory disease. Although the aetiology is obscure, Epstein–Barr virus infection may be responsible. Females are more commonly affected, in a 3:1 ratio.

Clinical features and treatment

1. **Presentation** is in the fourth decade with blurring of vision, which may be associated with floaters and photopsia.
2. **Signs**
   - Vitritis is universal; anterior uveitis is present in 50% of cases.
   - Multiple, discrete, small, round or ovoid, deep, yellowish-grey lesions located at the posterior pole and periphery (Fig. 10.125).
   - Other features include blind spot enlargement and occasionally mild disc oedema.

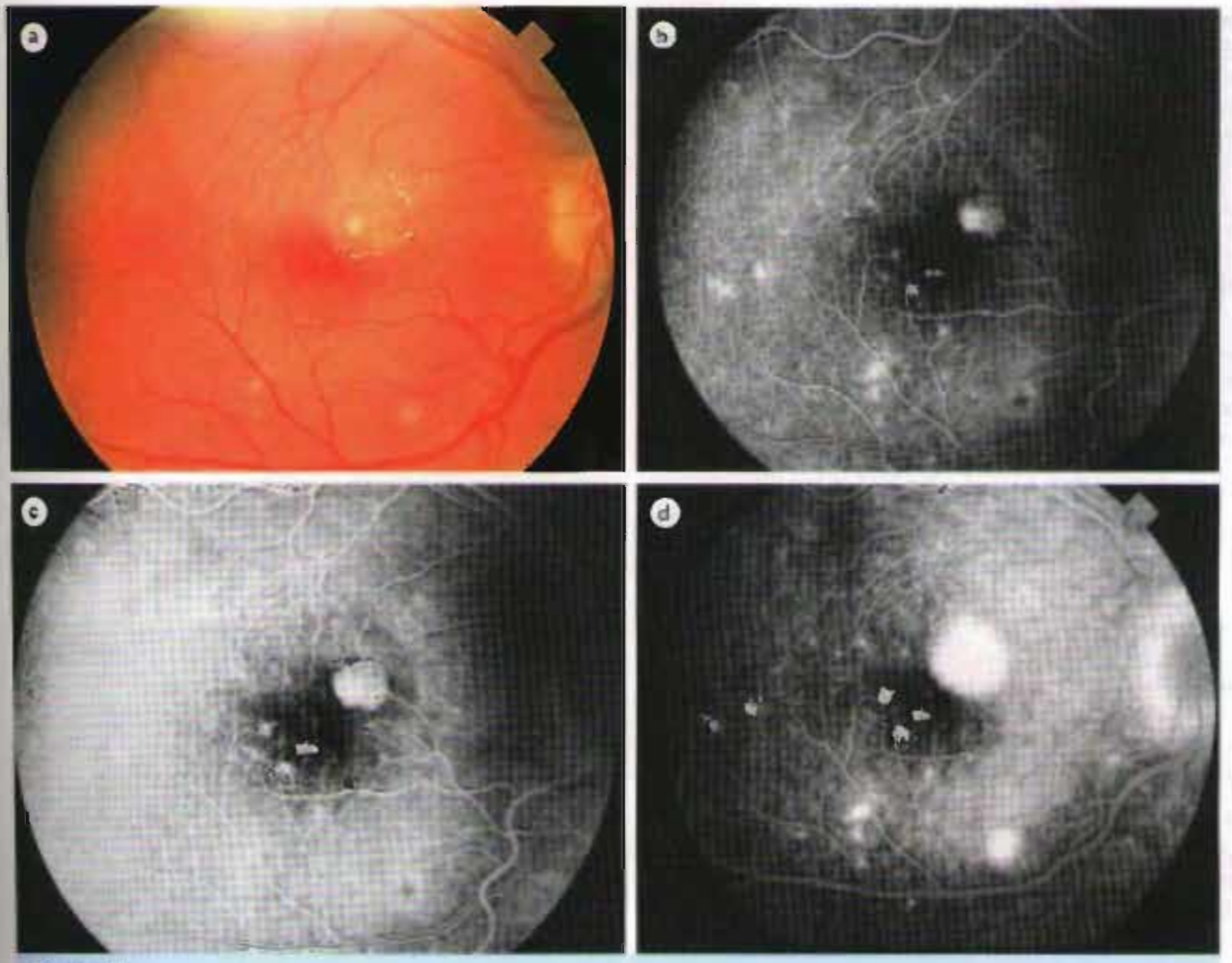


Fig. 10.124
Choroidal neovascularization in punctate inner choroidopathy (see text) (Courtesy of S. Milewski)

Fig. 10.125
Active multifocal choroiditis with panuveitis

3. **FA** of active lesions shows early blockage and late staining. Old inactive lesions show early hyperfluorescence which subsequently fades during the late phase.
4. **ERG** is normal or mildly subnormal.
5. **Course** may last many months with the development of fresh lesions and recurrent inflammatory episodes. Inactive lesions have sharp 'punched-out' margins and pigmented borders (Fig. 10.126). The prognosis is guarded because central vision may be impaired by direct foveal involvement, secondary CNV associated with a scar, CMO and occasionally diffuse subretinal fibrosis (Fig. 10.127).
6. **Treatment** with systemic steroids is effective in at least 50% of cases, although immunosuppressive agents are often necessary to reduce the complications of long-term systemic steroid therapy. Eyes with CNV may require laser photocoagulation.

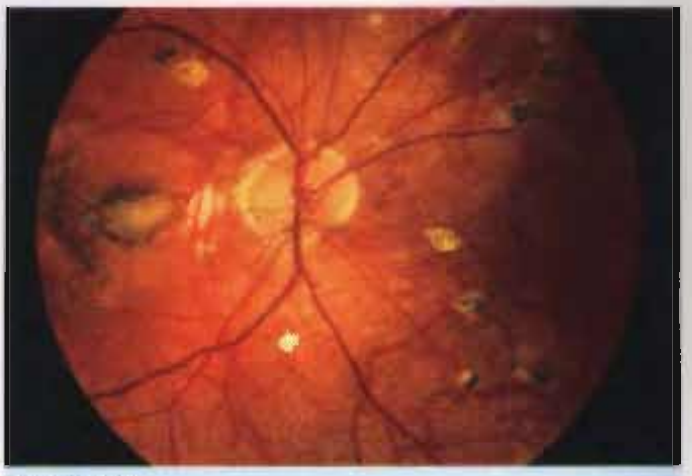


Fig. 10.126
Inactive multifocal choroiditis with panuveitis

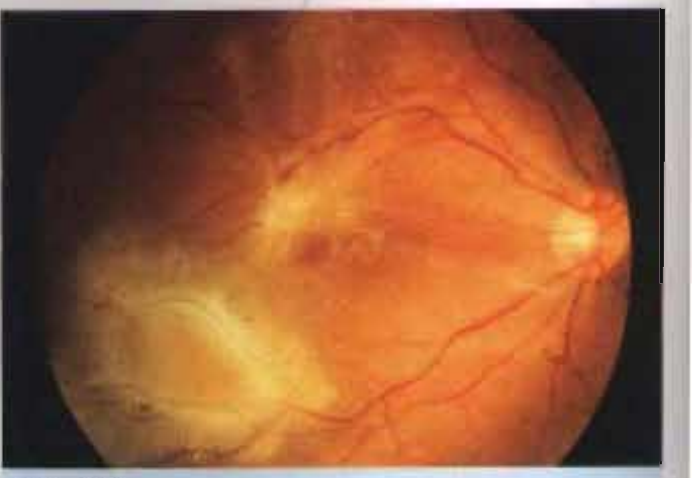


Fig. 10.127
Diffuse subretinal fibrosis

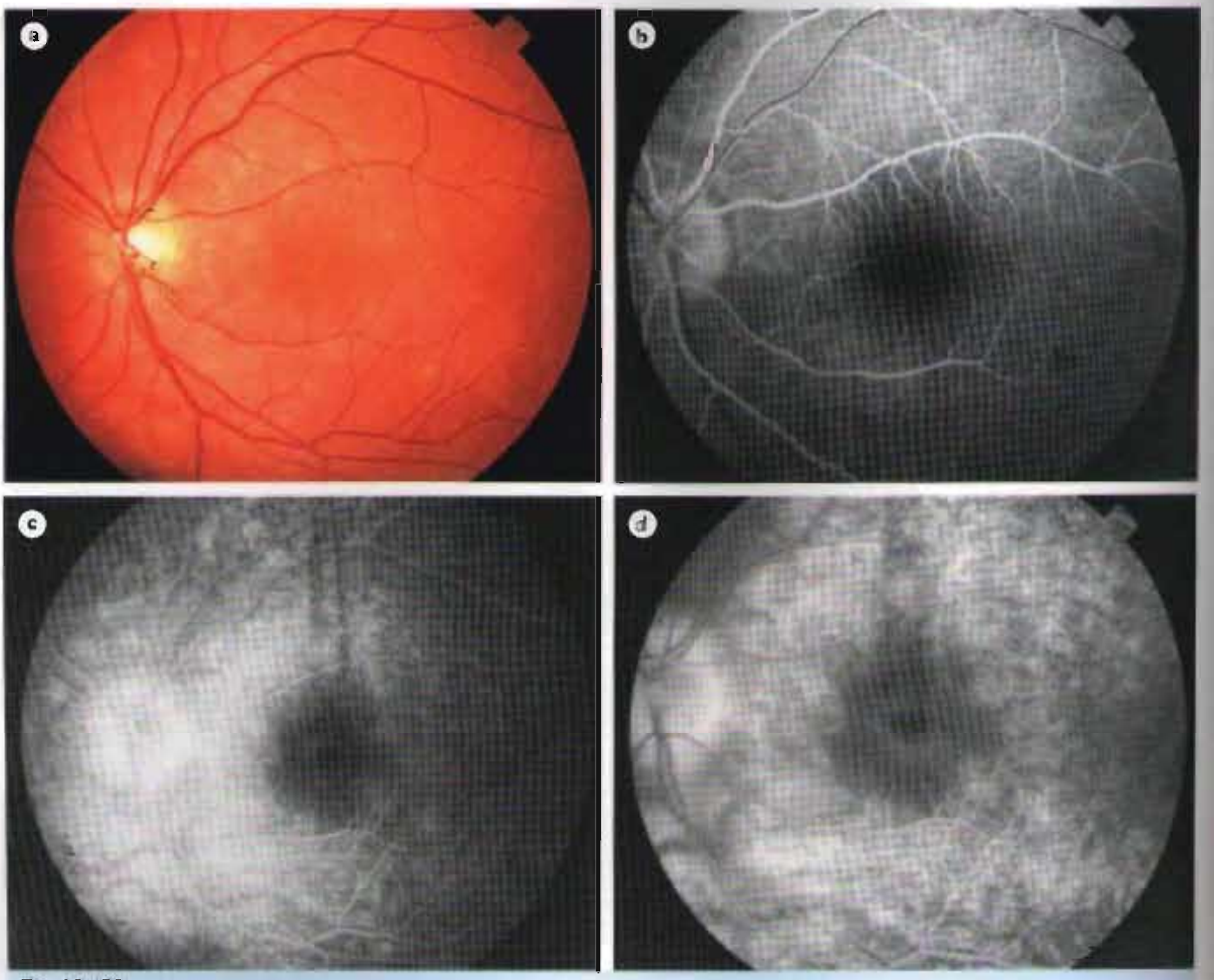


Fig. 10.128
Multiple evanescent white dot syndrome (*see text*) (Courtesy of S. Milewski)

Differential diagnosis

1. **Sarcoidosis**
   - Similarities: multifocal choroiditis and panuveitis.
   - Differences: lesions are usually more numerous in the inferior fundus and CNV does not develop.
2. **Ocular histoplasmosis**
   - Similarities: multifocal punched-out chorioretinal scars and CNV.
   - Differences: absence of intraocular inflammation and fresh lesions do not develop.
3. **Punctate inner choroidopathy**
   - Similarities: multifocal choroidal lesions and CNV.
   - Differences: absence of intraocular inflammation, peripheral involvement and preponderance for young myopic females.

Multiple evanescent white dot syndrome

Multiple evanescent white dot syndrome (MEWDS) is an uncommon, idiopathic, self-limiting, usually unilateral, inflammatory disease. Females are more commonly affected than males, in a 4:1 ratio. Although there is no treatment the prognosis is excellent. It is important to be aware of MEWDS because the subtle signs may be overlooked and misdiagnosis made of a more serious disorder such as retrobulbar neuritis, with its possible implications.

1. **Presentation** is in the third to fifth decades with sudden decreased vision which may be associated with photopsia typically affecting the temporal visual field. In some patients this is preceded by flu-like symptoms.

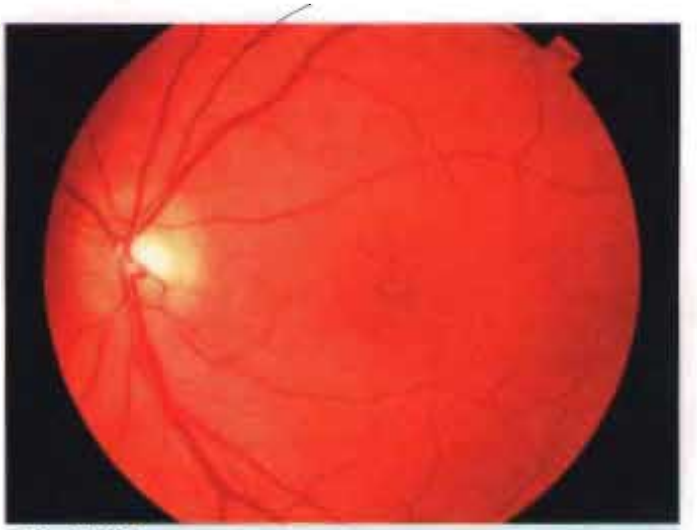


Fig. 10.129
Residual foveal granularity following resolved multiple evanescent white dot syndrome (Courtesy of S. Milewski)

2. **Signs**
   - Numerous, very small, deep, white dots involving the posterior pole but sparing the fovea (Fig. 10.128a). The fovea has a granular appearance which renders the foveal reflex abnormal or absent.
   - Mild vitritis and vasculitis.
   - Optic disc oedema and enlargement of the blind spot.
3. **FA** of active lesions shows a normal early phase (Fig. 10.128b). The late phase shows hyperfluorescence which may have a 'wreath-like' appearance (Fig. 10.128c and d).
4. **ERG** shows a decrease in a-wave amplitude.
5. **Course.** After a few weeks visual acuity recovers, the white dots fade and the disc oedema resolves. The fovea, however, retains its abnormal appearance (Fig. 10.129).

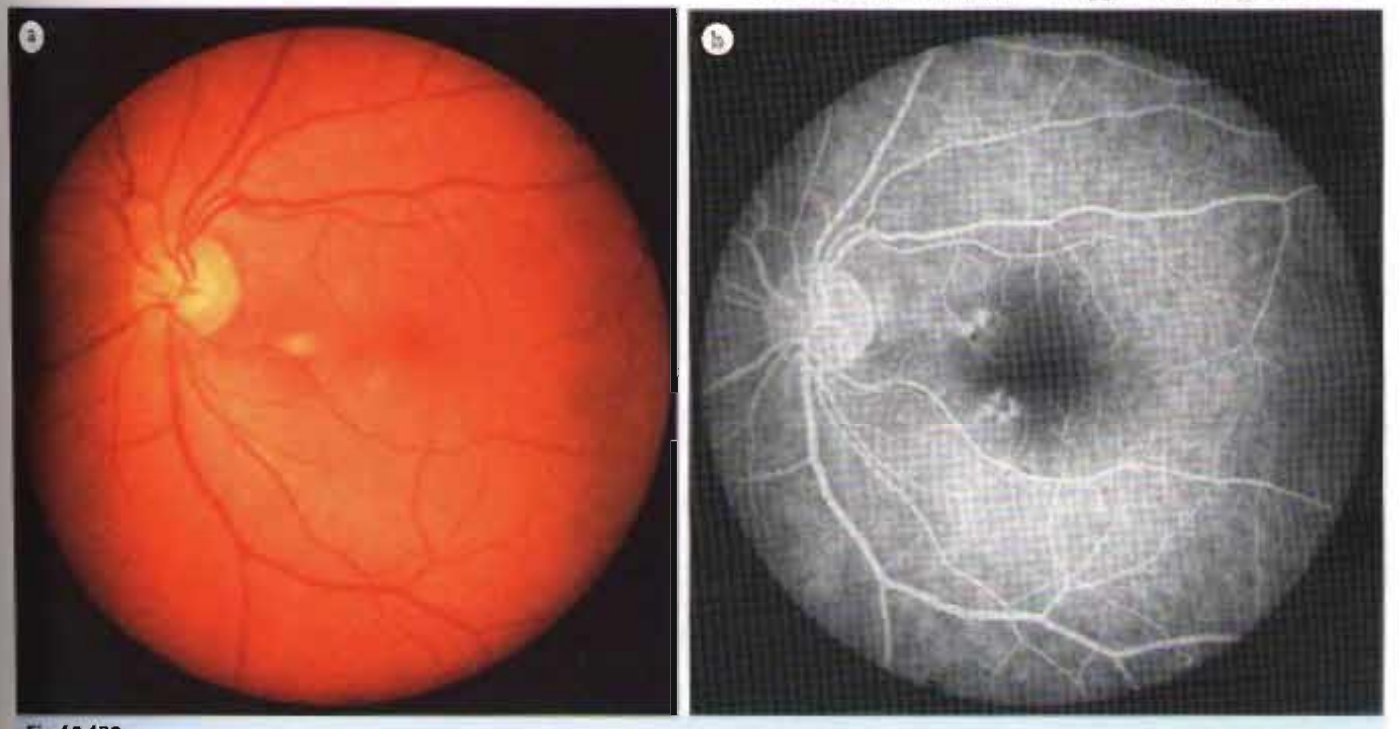


Fig. 10.130
Acute retinal pigment epitheliitis (see text) (Courtesy of M. Frost)

Acute retinal pigment epitheliitis

Acute retinal pigment epitheliitis is a rare, idiopathic, self-limiting inflammatory condition of the macular RPE. Although there is no treatment the visual prognosis is excellent. The condition is unilateral in 75% of cases and there is absence of intraocular inflammation.

1. **Presentation** is in the third to fifth decades with sudden impairment of central vision which may be associated with metamorphopsia.
2. **Signs**. The fovea shows a blunted reflex, with discrete clusters of a few, subtle, small, brown or grey spots at the level of the RPE which may be surrounded by hypopigmented yellow haloes (Fig. 10.130a).
3. **FA** shows small hyperfluorescent dots with hypofluorescent centres ('honeycomb' appearance) without leakage (Fig. 10.130b).
4. **EOG** is subnormal.
5. **Course**. Within 6–12 weeks the acute fundus lesions resolve and visual acuity returns to normal. Innocuous residual pigment clumping at the fovea may remain.

CHAPTER 11

Intraocular Tumours

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Iris tumours

Iris melanoma

In general, uveal melanomas are three times commoner in patients with blue/grey than brown irides. They are extremely rare in black people and there is no sexual predilection. Conditions associated with or predisposed to early-onset uveal melanomas are: (a) *ocular melanocytosis*, (b) *naevus of Ota*, (c) *dysplastic cutaneous naevi*, (d) *familial melanoma* and (e) *neurofibromatosis-1*. Iris melanoma makes up about 5% of uveal melanomas. The majority are composed of spindle B cells (*see* below) and are of low malignancy. A minority contain an epithelioid cell component and can be aggressive. The tumour usually grows very slowly along the iris surface and may invade the angle and anterior ciliary body. The prognosis is very good and only about 5% of patients develop metastases.

Clinical features

1. **Presentation** is in the fifth to sixth decades, a decade earlier than ciliary body and choroidal melanoma, with enlargement of a pre-existing iris lesion.
2. **Signs**
   a. Typical
   - A pigmented or non-pigmented nodule at least 3 mm in diameter and 1 mm thickness located in the *inferior half* of the iris with a smooth or irregular surface (Fig. 11.1). Surface vascularity is also present and is easier to detect in a non-pigmented (Fig. 11.2) than a highly pigmented tumour, where it may be masked.
   - Pupillary distortion, ectropion uveae and occasionally localized cataract may be seen (Fig. 11.3).
   - Features associated with a prominent epithelioid cell component include prominent vascularity, rapid growth and heterogeneous pigmentation.

Fig. 11.2
Non-pigmented iris melanoma with prominent surface vessels

Fig. 11.3
Iris melanoma causing distortion of the pupil, ectropion uveae and a localized lens opacity

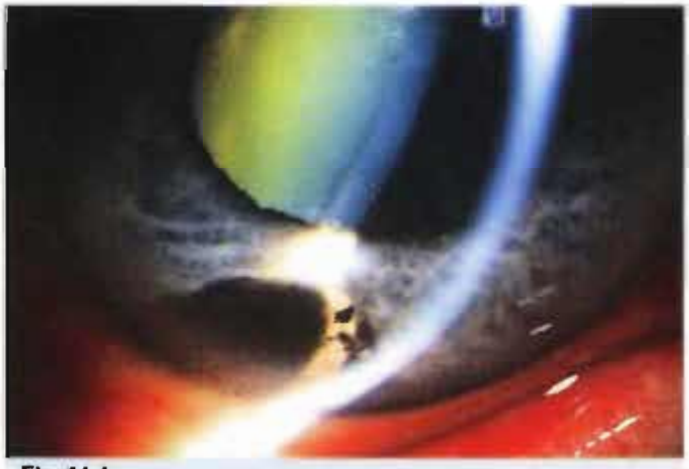

Fig. 11.1
Pigmented iris melanoma

Fig. 11.4
Tapioca iris melanoma (Courtesy of B. Damato)

b. Rare variants

- Diffusely growing intrastromal melanoma may give rise to ipsilateral hyperchromic heterochromia.
- 'Tapioca melanoma' is characterized by multiple surface nodules (Fig. 11.4).

Treatment

1. **Observation** of suspicious lesions involves documentation by slit-lamp examination, gonioscopy and photography. Follow-up should be lifelong because growth may occur after several years of apparent inactivity. Initially the patient is reviewed after 3–6 months, then 6–9 months and later annually.
2. **Iridectomy** for small tumours with iris reconstruction to reduce postoperative photophobia.
3. **Iridocyclectomy** for tumours invading the angle (Fig. 11.5).
4. **Radiotherapy** with local plaques (brachytherapy) or external irradiation with charged particles for non-resectable tumours.
5. **Enucleation** may be required for diffusely growing tumours.

Differential diagnosis

1. **Iris naevus**, if large and distorting the pupil (*see* Fig. 11.11).
2. **Ciliary body melanoma** with extension through the iris root (*see* Fig. 11.24).
3. **Metastasis** to the iris is rare and usually occurs in patients with a known systemic malignancy. It is a pink or yellow, fast-growing mass (Fig. 11.6) which may be associated with anterior uveitis and occasionally hyphaema. Small, multiple deposits may also be seen (Fig 11.7).
4. **Adenoma of the iris pigment epithelium** is a rare benign tumour characterized by a dark grey-black nodule with a smooth but sometimes multinodular surface, most frequently in the peripheral iris (Fig. 11.8). The lesion causes anterior displacement and thinning of the iris stroma, which eventually erodes, disclosing the tumour on slit-lamp biomicroscopy.
5. **Leiomyoma** is an extremely rare benign tumour which arises from smooth muscle. The appearance is similar to that of an amelanotic melanoma except that it is not necessarily confined to the inferior half of the iris (Fig. 11.9). Often the diagnosis can be established only histologically.
6. **Primary iris cyst** (*see* below).

Fig. 11.5
Gonioscopic view of iris melanoma involving the angle

Fig. 11.7
Multiple iris metastases (Courtesy of B. Damato)

Fig. 11.6
Solitary iris metastasis

Fig. 11.8
Adenoma of the iris pigment epithelium

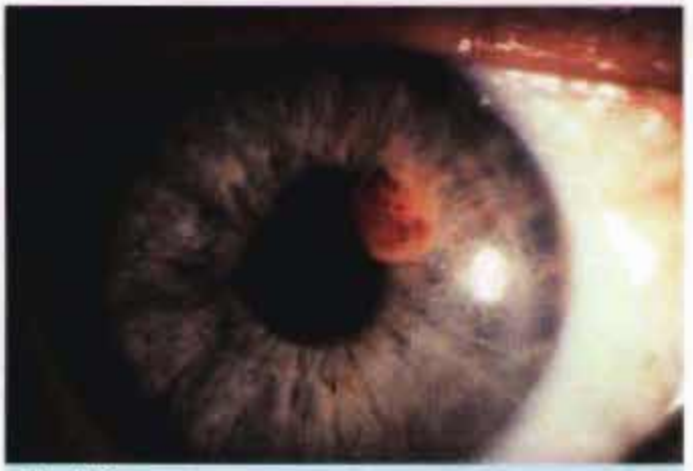

Fig. 11.9
Iris leiomyoma

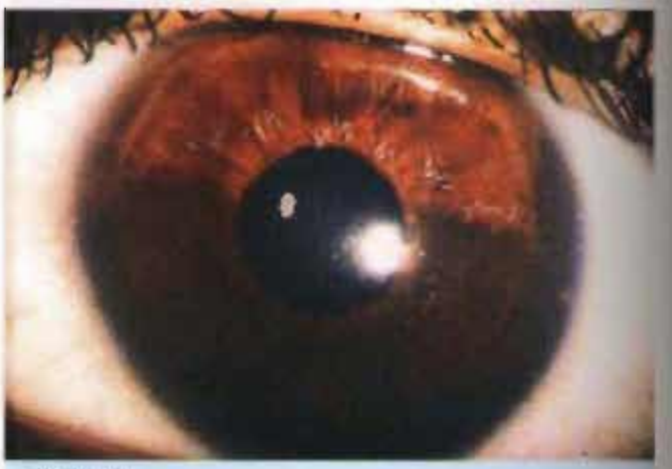

Fig. 11.12
Diffuse iris naevus

Fig. 11.10
Iris naevus and freckles

Fig. 11.13
Lisch nodules

Fig. 11.11
Iris naevus distorting the pupil

Iris naevi

1. **A typical naevus** is a pigmented, flat or slightly elevated lesion, usually less than 3mm in diameter (Fig. 11.10). It is located in the superficial layers and may occasionally cause mild distortion of the pupil and ectropion uveae (Fig. 11.11).
2. **A diffuse naevus** obscures normal iris crypts and gives rise to hyperchromic heterochromia (Fig. 11.12). It may be seen in patients with the *Cogan–Reese syndrome* (see Chapter 9) and may also show small pedunculated nodules resembling mammillations.
3. **Lisch nodules** are multiple, small, bilateral, melanocytic hamartomas found after the age of 16 years in virtually all patients with neurofibromatosis-1 (Fig. 11.13).
4. **Freckles** are smaller than naevi (*see* Fig. 11.10). They are frequently multiple and bilateral, but never distort the iris architecture.

Iris cysts

Primary cysts

Primary iris cysts are rare curiosities arising from the pigment epithelium or, rarely, the stroma. The vast majority

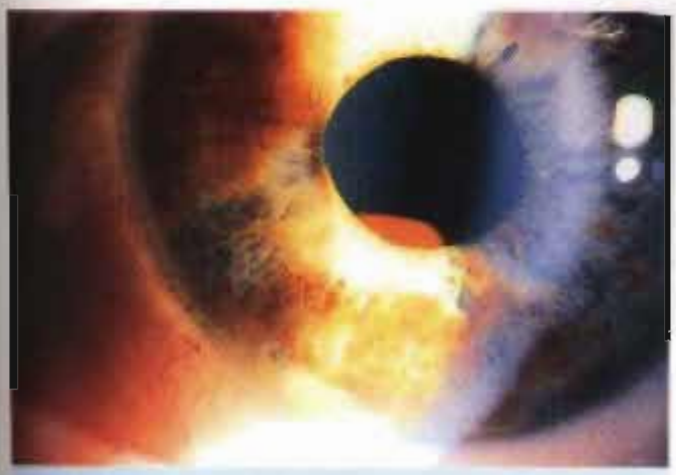

Fig. 11.14
Pupillary epithelial iris cyst

Fig. 11.15
Mid-zonal epithelial iris cyst

Fig. 11.16
Primary stromal iris cyst

Fig. 11.17
Primary stromal iris cyst containing a fluid–debris level

particularly those arising from the pigment epithelium, are stationary and asymptomatic.

1. **Epithelial** cysts are unilateral, solitary, dark-brown, globular structures which transilluminate. They may be located at the pupillary border (Fig. 11.14), in the mid-zone (Fig. 11.15) or the iris root. Occasionally the cysts become dislodged and float freely in the anterior chamber or vitreous. The vast majority are innocuous and rarely require treatment.
2. **Stromal** cysts present in the first year of life. They are solitary, unilateral, have a smooth, translucent anterior wall and contain fluid (Fig. 11.16). The cyst may remain dormant for many years or suddenly enlarge and cause secondary glaucoma, corneal decompensation and show a fluid–debris level reminiscent of a pseudo-hypopyon (Fig. 11.17). Occasionally the cyst may break free from the iris and float in the anterior chamber or migrate to another location. Although spontaneous regression can occur, most require treatment by needle aspiration or surgical excision.

Fig. 11.18
Secondary iris cyst containing a worm

Secondary cysts

Secondary iris cysts develop as a result of implantation, parasites (Fig. 11.18), tumours or the prolonged use of

Fig. 11.19
Secondary iris cysts due to topical administration of long-acting miotics

Fig. 11.20
Secondary iris cyst following corneal grafting

Fig. 11.21
Sentinel vessels associated with ciliary body melanoma
(Courtesy of B. Damato)

long-acting miotics. The latter are usually bilateral, small, multiple and located along the pupillary border (Fig. 11.19). Their development can be prevented by the use of topical 2.5% phenylephrine. Implantation cysts originate by deposition of surface epithelial cells from the conjunctiva or cornea on the iris after penetrating or surgical trauma and may lead to the following:

1. **Pearl** cysts are small, white, solid lesions with opaque walls located in the stroma and are not connected to the wound.
2. **Serous** cysts are translucent, filled with fluid and may be connected to the wound (Fig. 11.20). They frequently enlarge, leading to corneal oedema, anterior uveitis and glaucoma. Ultrasound biomicroscopy may show the location and extent of the lesions when surgical excision is contemplated.

Ciliary body tumours

Ciliary body melanoma

About 10% of uveal melanomas arise from the ciliary body.

Clinical features

1. **Presentation** is in the sixth decade with visual symptoms but occasionally the tumour may be discovered incidentally
2. **Signs** depend on the size and location of the tumour. Small localized tumours cannot usually be visualized without pupillary dilatation and gonioscopy.
   - Dilated episcleral blood vessels in the same quadrant as the tumour (sentinel vessels) (Fig. 11.21).
   - Extraocular extension through the scleral emissary vessels may produce a dark episcleral mass (Fig. 11.22) which may be mistaken for a conjunctival melanoma.
   - Pressure on the lens may give rise to astigmatism, subluxation or cataract (Fig. 11.23).
   - Erosion through the iris root may mimic iris melanoma (Fig. 11.24).
   - Retinal detachment may be caused by posterior extension.

Fig. 11.22
Extraocular extension of ciliary body melanoma

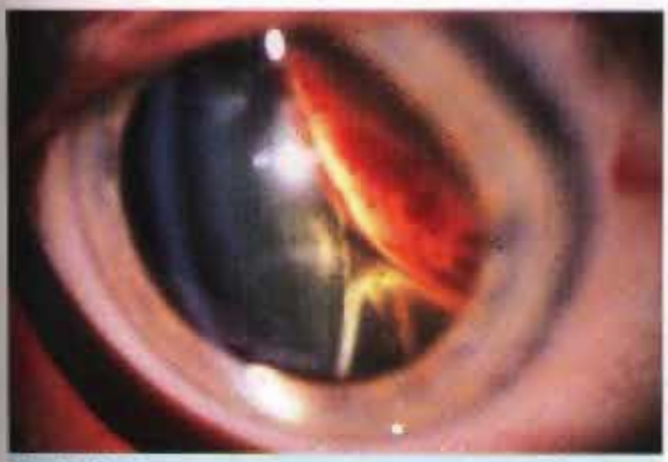

Fig. 11.23
Ciliary body melanoma displacing the lens (Courtesy of C. Barry)

Fig. 11.24
Ciliary body melanoma eroding the iris root

- Anterior uveitis, caused by tumour necrosis, is uncommon.
- Circumferential (annular) growth for 360° carries the worst prognosis because early diagnosis is difficult.

Investigations

1. **Triple-mirror contact lens** examination through a well-dilated pupil is essential and is particularly useful in detecting forward erosion through the iris root into the angle.
2. **Transillumination** may give an approximate indication of tumour extent but is of little diagnostic value because an amelanotic melanoma may transilluminate.
3. **Ultrasonic biomicroscopy** is useful in eyes with opaque media and also shows dimensions and extent.
4. **Biopsy** may be helpful in selected cases.

Treatment

1. **General considerations** (*see* choroidal melanoma below).
2. **Enucleation** for large tumours and those affecting the anterior choroid. Secondary glaucoma, resulting from extensive invasion of Schlemm canal, is also an indication for enucleation.
3. **Iridocyclectomy** for small or medium-sized tumours involving no more than one-third of the angle. Complications are vitreous haemorrhage, retinal detachment and incomplete resection.
4. **Radiotherapy** by brachytherapy or external beam irradiation in selected cases.

Differential diagnosis

1. **Uveal effusion syndrome** (*see* Fig. 12.66) may resemble circumferential ciliary body melanoma. However, the effusion is lobulated, transilluminates brightly and appears cystic on ultrasonography.
2. **Congenital epithelial iridociliary cysts** may displace the lens but can be readily differentiated from melanomas by ultrasonography.
3. **Other ciliary body tumours**, which are extremely rare, include medulloepithelioma, metastases, adenocarcinoma, cystic adenoma and leiomyoma. In most of these the correct diagnosis can be made only histologically.

Choroidal tumours

Choroidal melanoma

Melanoma of the choroid is the most common primary intraocular tumour in adults and accounts for 85% of uveal melanomas.

Clinical features

1. **Presentation** is usually during the sixth decade (range fifth to eighth) in one of the following ways:

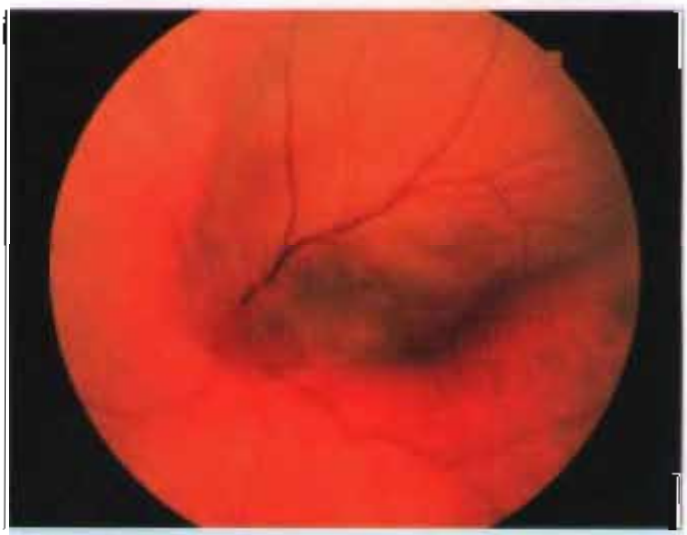

Fig. 11.25
Choroidal melanoma

- An asymptomatic tumour detected by chance.
- A symptomatic tumour causing decreased visual acuity or a visual field defect.
- About a third of patients complain of very brief 'balls of light' travelling across the visual field two to three times a day, most apparent in subdued lighting.

2. **Signs**
   - An elevated, subretinal, dome-shaped, brown or grey mass (Fig. 11.25). Occasionally the tumour may be mottled with dark-brown or black pigment, or be virtually amelanotic (Fig. 11.26). Surface orange pigment (lipofuscin) is common but not diagnostic.
   - If the tumour breaks through Bruch membrane it acquires a mushroom-shaped appearance (Fig. 11.27).

Fig. 11.26
Amelanotic choroidal melanoma

Fig. 11.27
Mushroom-shaped choroidal melanoma with surface lipofuscin
(Courtesy of D. Lehman)

Fig. 11.28
B-scan ultrasonogram showing a choroidal melanoma and secondary retinal detachment

   - A secondary exudative detachment is common and must not be mistaken for a rhegmatogenous detachment.
   - Occasional features include choroidal folds, haemorrhage, secondary glaucoma, cataract and uveitis.

Investigations

1. **Binocular indirect ophthalmoscopy** is sufficient for accurate diagnosis in the vast majority of cases.
2. **Indirect slit-lamp biomicroscopy** detects subtle features associated with relatively small tumours, such as the presence of lipofuscin pigment, subretinal fluid, cystoid changes in the overlying sensory retina and dilated vessels within the tumour.
3. **Ultrasonography** is used to determine tumour size and detect extraocular extension. B-scan ultrasonography shows the anterior border of the tumour as well as acoustic hollowness, choroidal excavation and orbital shadowing (Fig. 11.28).
4. **FA** is of limited diagnostic value because there is no pathognomonic pattern. Most melanomas show a 'dual circulation' (Fig. 11.29b and c), mottled fluorescence during the arteriovenous phase and progressive leakage and staining (Fig. 11.29d).
5. **ICG** is superior to FA because there is less interference caused by RPE changes, better visualization of the tumour and choroidal vessels, and superior definition of tumour margins.
6. **MRI**, particularly when combined with surface coils and fat suppression sequences, shows that choroidal melanomas are hyperintense in T1-weighted (Fig. 11.30) and hypointense in T2-weighted images, but these features are not pathognomonic.
7. **Colour-coded Doppler** imaging may differentiate pigmented tumours from intraocular haemorrhage, particularly in eyes with opaque media.
8. **Fine-needle aspiration biopsy** is used occasionally to obtain cellular aspirates for analysis where the diagnosis cannot be established by less invasive methods.

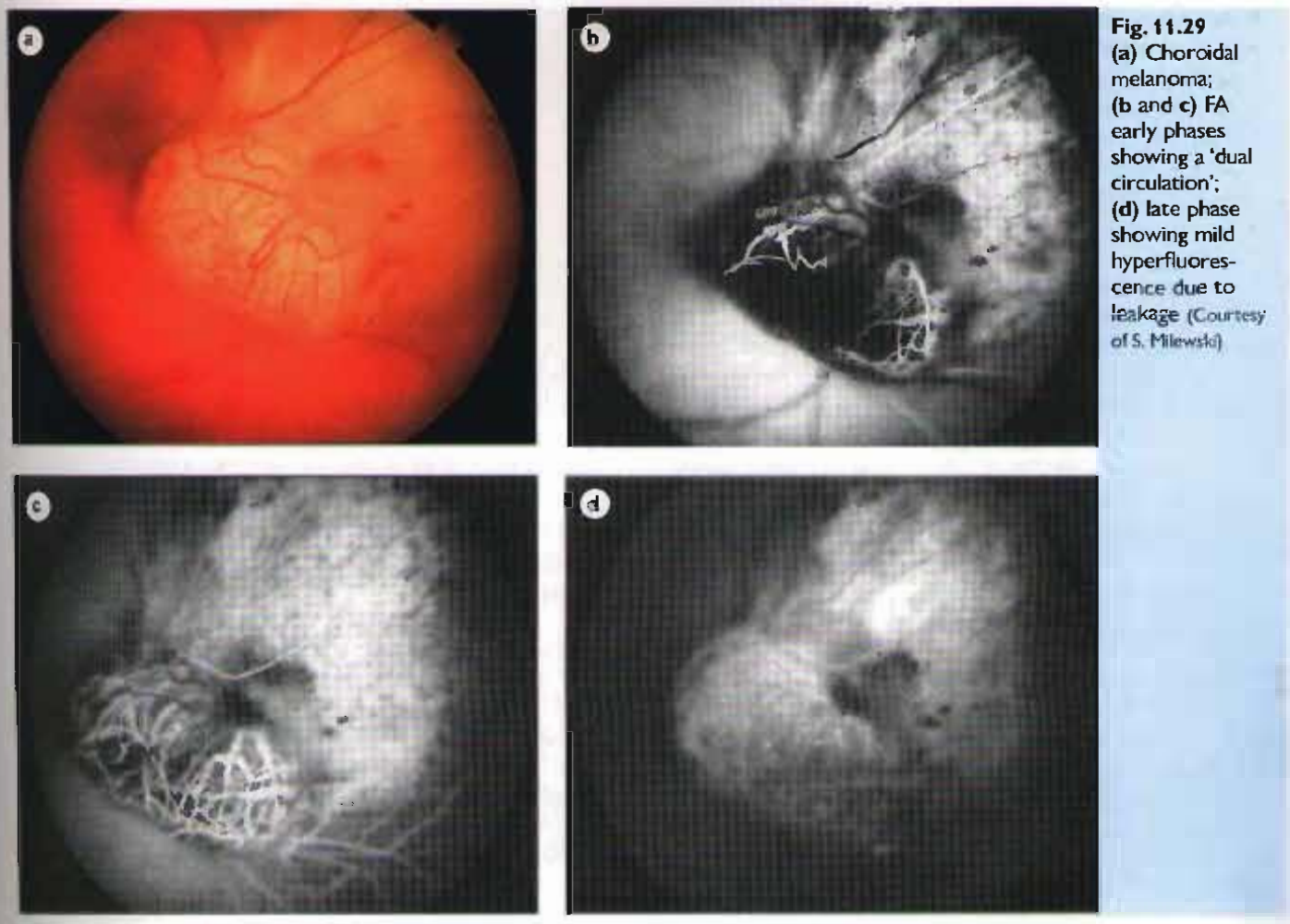

Fig. 11.29
(a) Choroidal melanoma; (b and c) FA early phases showing a 'dual circulation'; (d) late phase showing mild hyperfluorescence due to leakage (Courtesy of S. Milewski)

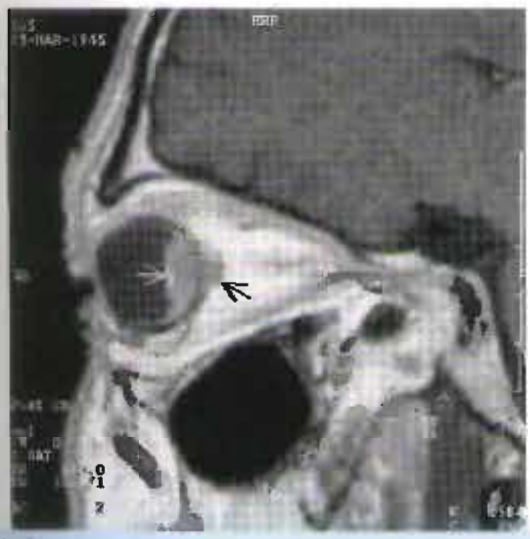

Fig. 11.30
T1-weighted MRI scan showing a choroidal melanoma (white arrow) and extraocular extension (black arrow) (Courtesy of M Karolczak-Kulesza)

9. **General medical examination** is aimed at:
   - Excluding a metastasis to the choroid, which occurs most frequently from the bronchus in both sexes and the breast in women. Occasionally, the primary site is the kidney or gastrointestinal tract. Initial investigations should include chest radiography, rectal examination and mammography in females.
   - Detecting metastatic spread *from* the choroid as this would influence management. For example, a patient with overt metastatic disease would not be subjected to enucleation of a painless eye. The liver is by far the most frequent site for metastases. Hepatic involvement can be detected by ultrasonography and elevated gamma-glutamyl transpeptidase and alkaline phosphatase levels. Chest radiography should also be performed to detect possible lung secondaries but these are rare without liver metastases.

Treatment

This is complex and should be tailored to the individual patient. The following factors are considered: (a) size, location, extent and apparent activity of the tumour, (b) state of the fellow eye, (c) general health and age of the patient and (d) the patient's wishes and fears. For instance, treatment may be inappropriate for a slowly growing tumour in the only eye of a very elderly or chronically ill patient. There is an increasing trend towards the use of combined therapy with the following modalities:

1. **Brachytherapy** is frequently the treatment of first choice because it is relatively straightforward and effective.
   a. ***Indications*** are tumours less than 10 mm in elevation and less than 20 mm in basal diameter in which there is a reasonable chance of salvaging vision. Supplemental transpupillary thermotherapy may be required to enhance the results. Tumour regression starts about 1–2 months after treatment and continues for several years.
   b. ***Complications*** include retinopathy, papillopathy, vitreous haemorrhage, cataract and recurrence of tumour.
   c. ***Cure rate*** is similar to that following enucleation of comparable tumours.
2. **External radiotherapy** with protons or helium ions by means of a cyclotron unit. The advantages over brachytherapy are that the beam can be more highly focused, affording a more homogeneous dose of radiation. Treatment is fractionated over 4 days, with each dose delivered over a 30-second period.
   a. ***Indications*** are tumours unsuitable for brachytherapy either because of size or posterior location to within 4 mm of the disc or fovea.
   b. ***Complications***, which are more common following treatment of large tumours, include loss of lashes, eyelid depigmentation, canaliculitis with epiphora, conjunctival keratinization, keratitis, exudative retinal detachment and neovascular glaucoma.
   c. ***Cure rate*** is similar to that following brachytherapy or enucleation.
3. **Transpupillary thermotherapy** (TTT) is performed with a diode laser to induce hyperthermia but not coagulation.
   a. ***Indications*** are selected small tumours, particularly if pigmented and located near the fovea or optic disc. TTT is also a complementary modality to brachytherapy.
   b. ***Complications*** include visual field defects and maculopathy.
4. **Trans-scleral local resection** is a difficult procedure which involves excision of the tumour with a rim of healthy choroid under a partial-thickness scleral flap. The procedure is performed under systemic arterial hypotension.
   a. ***Indications*** are carefully selected tumours that are too thick for radiotherapy and usually less than 16mm in diameter.
   b. ***Complications*** include haemorrhage, retinal detachment, cataract and tumour recurrence.
5. **Stereotactic radiosurgery** with the Gamma-knife is a new method involving single-session delivery of ionizing radiation to a stereotactically localized volume of tissue. This modality is an alternative to charged particle irradiation or enucleation in treating large tumours with preservation of visual function in selected cases.
6. **Enucleation**
   a. ***Indications*** for excision of the globe are very large tumours, particularly if all useful vision has been irreversibly lost. In these cases, enucleation is preferred to brachytherapy because the dose of radiation required to reach the apex of the tumour would be too great to salvage the rest of the globe.
   b. ***Technique*** should be meticulous to avoid dissemination of malignant cells. The procedure should be performed with gentle isolation and section of the extraocular muscles, and minimal traction on the optic nerve when cutting. About 4 weeks after enucleation, the patient can be fitted with an artificial eye.
7. **Exenteration** of the orbit is indicated for patients with extensive extraocular extension at the time of diagnosis or for orbital recurrences following enucleation.
8. **Palliation** with chemotherapy and/or immunotherapy may prolong life in patients with metastatic disease. In patients with lung metastases, life expectancy is generally <1 year and, when the liver is involved, <6 months.

Modified Callender classification of uveal melanomas

1. **Spindle cell melanomas**, which make up 45% of all tumours, are composed of spindle cells, with a small proportion described as fascicular because of the palisading or ribbon-like arrangement of cells in parallel rows (Fig. 11.31).
2. **Pure epithelioid cell melanomas** make up 5% (Fig. 11.32).
3. **Mixed cell melanomas**, containing spindle and epithelioid cells, account for 45% (Fig. 11.33).
4. **Necrotic melanomas**, in which the predominant cell type is unrecognizable, make up the remaining 5% (Fig. 11.34).

Prognostic factors

1. **Histological features** implying an adverse prognosis include large numbers of epithelioid cells per high-power field, closed vascular loops within the tumour and lymphocytic infiltration.

Fig. 11.31
Fascicular spindle cell melanoma (Courtesy of A. Garner)

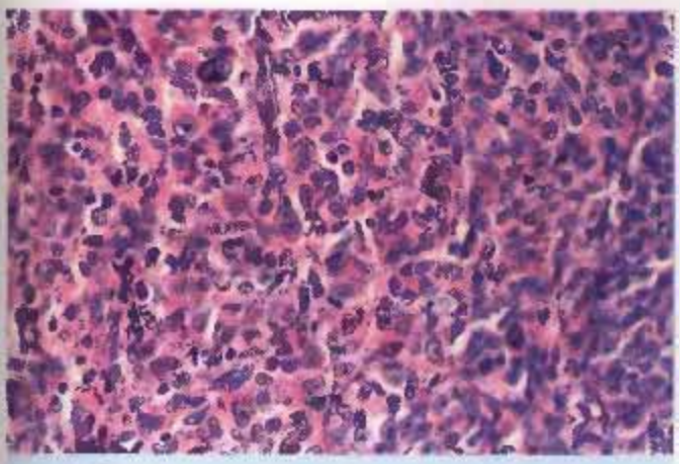

Fig. 11.32
Epithelioid cell melanoma (Courtesy of A. Garner)

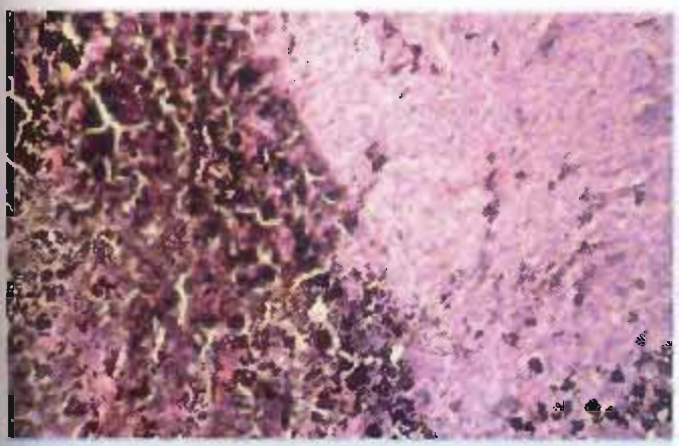

Fig. 11.33
Mixed cell melanoma (Courtesy of A. Garner)

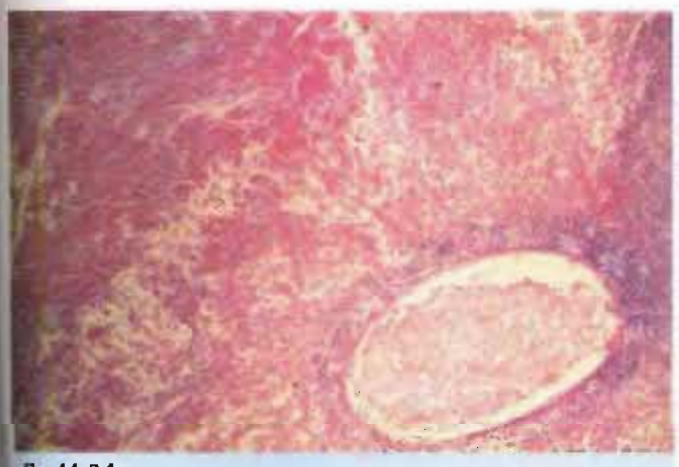

Fig. 11.34
Necrotic melanoma (Courtesy of A. Garner)

2. **Chromosomal abnormalities** within the melanoma cells are associated with a very poor prognosis, with a 50% death rate at 5 years.
3. **Large tumours** have a worse prognosis than small tumours. Following enucleation, 5-year mortality is as follows:
   - Small tumours (<10 mm in diameter): 16%.
   - Medium tumours (10–15 mm in diameter): 32%.
   - Large tumours: 53%.
4. **Extrascleral extension** carries a very poor prognosis.
5. **Location**: anterior tumours have a worse prognosis because they are usually diagnosed later than those near the posterior pole.
6. **Patients over the age of 65 years** have a worse prognosis than younger patients.

Differential diagnosis

Although in the vast majority of cases the diagnosis is straightforward, the following conditions should be considered in the differential diagnosis of atypical cases, particularly amelanotic melanomas:

1. **Other choroidal tumours**, most notably large naevi, circumscribed haemangiomas and solitary metastases.
2. **Solitary choroidal granulomas** associated with sarcoidosis or tuberculosis.
3. **Posterior scleritis** (*see* Chapter 7).

Choroidal naevus

Choroidal naevi are present in about 5% of the general population but are less common in fair-skinned individuals. Although they are probably present at birth, growth occurs mainly during the pre-pubertal years and is extremely rare thereafter. For this reason the rare event of clinically detectable growth should arouse suspicion of malignant transformation.

Signs

1. **Typical naevus**
   - An asymptomatic, oval or circular, slate-blue or green-grey lesion with detectable but not sharp borders which may be associated with surface drusen (Fig. 11.35 and *see* Fig. 11.38a).
   - Dimensions are <5 mm in diameter and 1 mm or less in thickness.
2. **A suspicious naevus** has one or more of the following characteristics:
   - Presence of symptoms, such as metamorphopsia or photopsia.
   - Dimensions >5 mm in diameter and >1 mm in thickness (Fig. 11.36).
   - Clumps of surface orange (lipofuscin) pigment (Fig. 11.37).
   - Absence of surface drusen on a thick lesion.
   - Location of the posterior margin of the lesion within 3 mm of the optic disc.
   - Serous retinal detachment either over the surface of the lesion or inferiorly.

NB: The greater the number of these features, the higher the chance that the lesion is a melanoma.

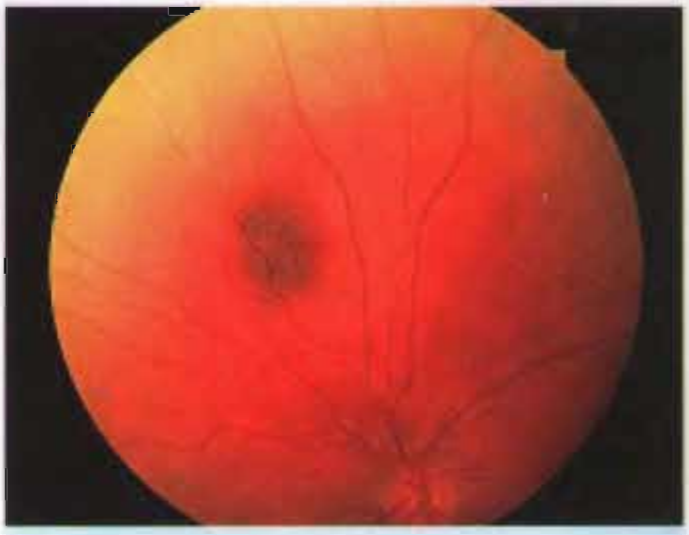

Fig. 11.35
Typical choroidal naevus

Fig. 11.36
Suspicious choroidal naevus

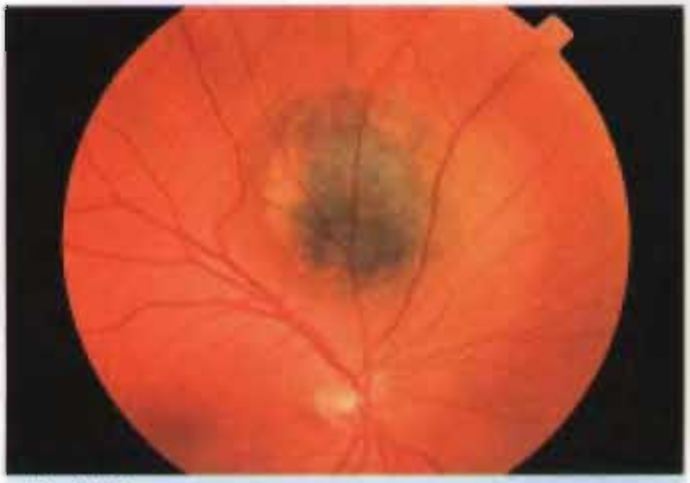

Fig. 11.37
Suspicious choroidal naevus with surface lipofuscin

Investigations

1. **FA** findings depend on the amount of pigmentation within the naevus and associated changes in the overlying RPE. Most choroidal naevi are avascular and pigmented, giving rise to hypofluorescence caused by blockage of background choroidal fluorescence. If the naevus is associated with surface drusen, this will result in areas of hyperfluorescence (Fig. 11.38b). FA is, however, not helpful in distinguishing a small melanoma from a naevus.
2. **Ultrasonography** shows a localized flat or slightly elevated lesion with high internal reflectivity (Fig. 11.39).

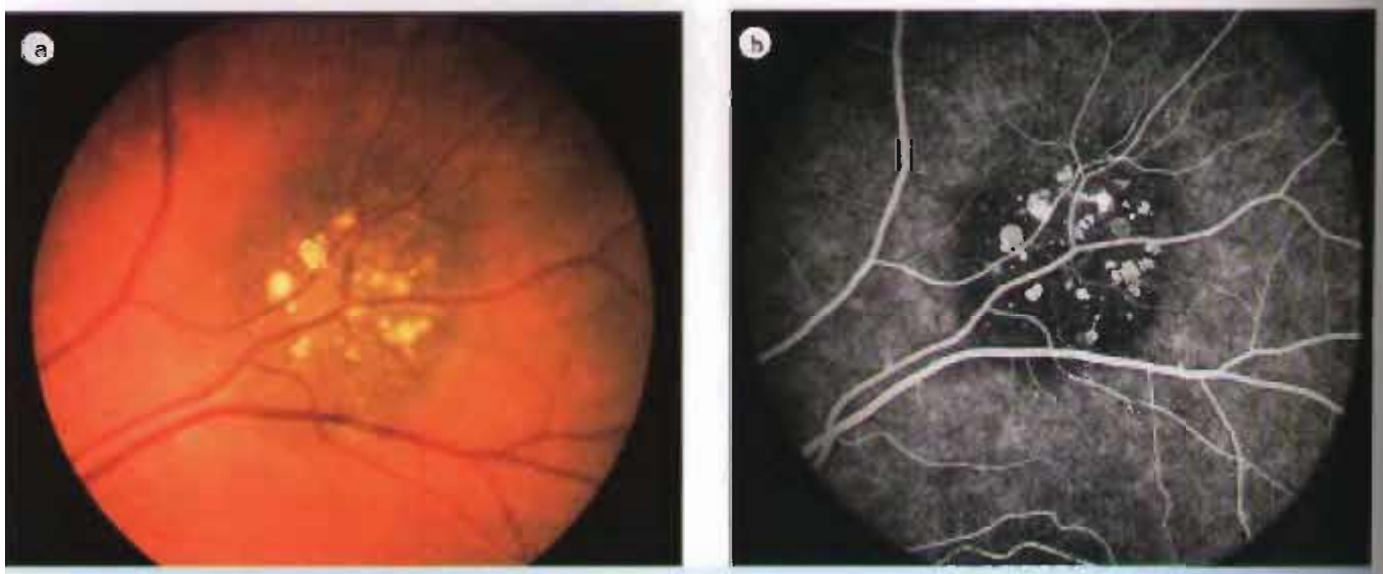

Fig. 11.38
(a) Typical choroidal naevus with surface drusen; (b) FA showing blockage of background fluorescence and hyperfluorescence of surface drusen

Fig. 11.39
B-scan ultrasonogram of choroidal naevus (see *text*) (Courtesy of M Karolczak-Kulesza)

Fig. 11.40
Circumscribed choroidal haemangioma (Courtesy of J.A. Shields and A. Singh)

Management

1. **Typical naevi** do not require follow-up because the risk of malignant transformation is extremely low.
2. **Suspicious naevi** should be evaluated initially every 3–6 months and then 9–12 months with fundus photography and ultrasonography to detect the possibility of growth. Although it is difficult to detect small changes in thickness by ultrasonography, careful comparison of fundus photographs, with special attention to the location of landmarks such as blood vessels, is usually a reliable method of documenting growth. Once growth has been documented, the lesion should be reclassified as a choroidal melanoma and managed accordingly.

Circumscribed choroidal haemangioma

Circumscribed choroidal haemangioma is a rare, benign, vascular hamartoma which is probably present at birth but does not become symptomatic until years later. The tumour is almost always solitary and is not associated with systemic disease. Most are stationary and a few are slow-growing.

Clinical features

1. **Presentation** is in the fourth to fifth decades with unilateral central visual impairment.
2. **Signs**
   - A dome-shaped or placoid, orange-red, mass which blends with the surrounding choroid (Fig. 11.40). Subtle white foci may be present on the surface of the tumour and probably represent fibrous metaplasia of the overlying RPE.
   - The lesion usually measures 3–9 mm in diameter and is most commonly located in the juxtapapillary or macular area.
3. **Complications** include secondary cystoid retinal degeneration overlying the tumour, exudative retinal detachment, macular invasion, RPE degeneration and subretinal fibrosis.

Special investigations

1. **Ultrasonography** shows an oval or placoid lesion with a sharp anterior border and high internal reflectivity, but no choroidal excavation or orbital shadowing (Fig. 11.41).
2. **FA** reveals filling during the choroidal phase (Fig. 11.42a), progressive hyperfluorescence during the venous phase and late leakage (Fig. 11.42b).

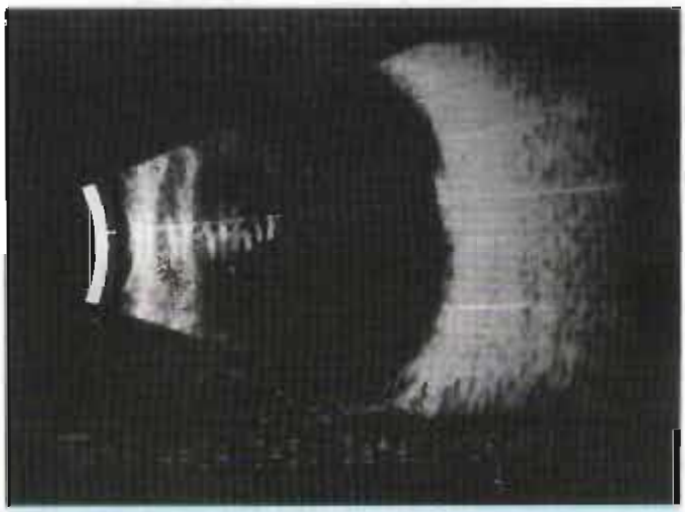

Fig. 11.41
B-scan ultrasonogram of circumscribed choroidal haemangioma (see *text*) (Courtesy of S. Milewski)

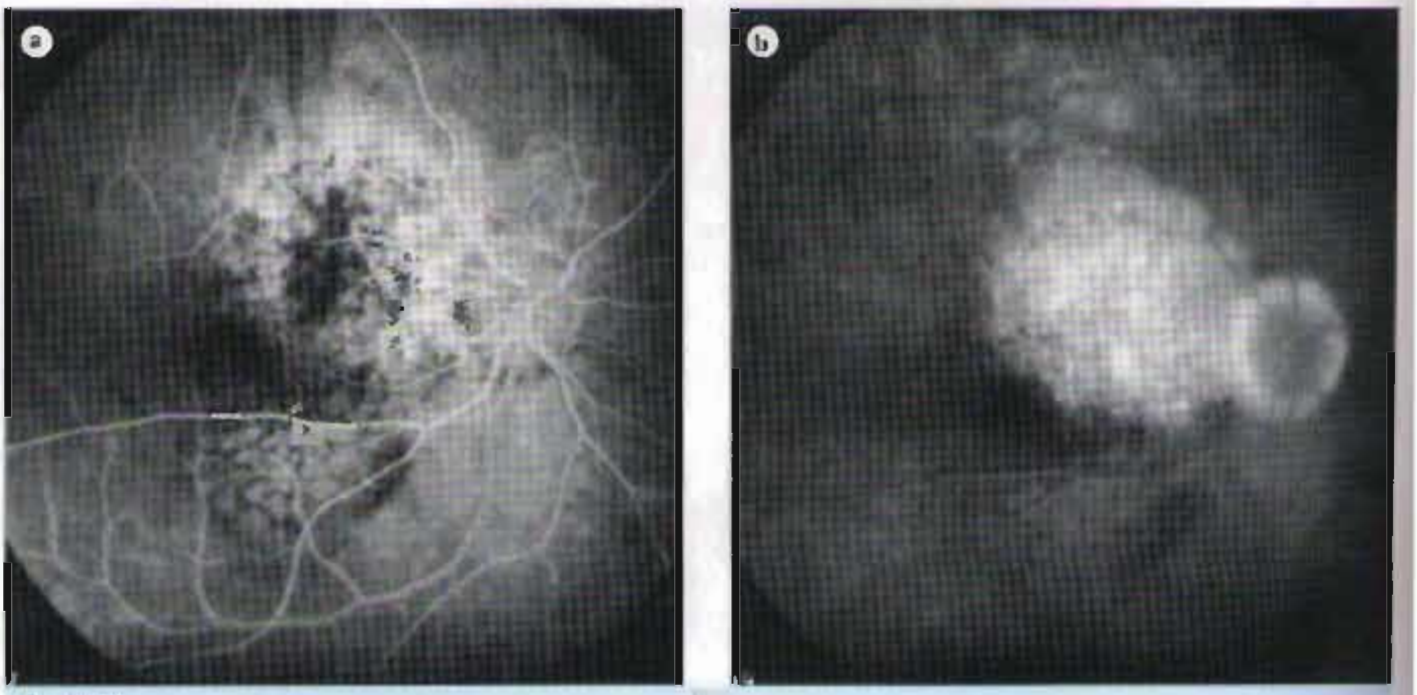

Fig. 11.42
FA of circumscribed choroidal haemangioma. (a) Early phase showing hyperfluorescence due to filling; (b) late phase showing leakage (Courtesy of S. Milewski)

Treatment

Vision-threatening lesions may be treated as follows:

1. **Transpupillary thermotherapy** for lesions not involving the macula. Indocyanine green can be administered as an adjunct to enhance uptake of diode laser energy.
2. **Radiotherapy** either by low-dose lens-sparing external beam irradiation or brachytherapy.

Diffuse choroidal haemangioma

The diffuse choroidal haemangioma usually affects over half of the choroid and enlarges very slowly. It occurs in patients with the Sturge–Weber syndrome ipsilateral to the naevus flammeus (*see* Chapter 20).

1. **Presentation** is in the third decade with visual impairment.
2. **Signs.** Thickening of the choroid and a deep-red 'tomato ketchup' colour which is most marked at the posterior pole (Fig. 11.43).
3. **Complications** include secondary retinal cystoid degeneration and exudative retinal detachment.
4. **Treatment** is by external beam radiotherapy.

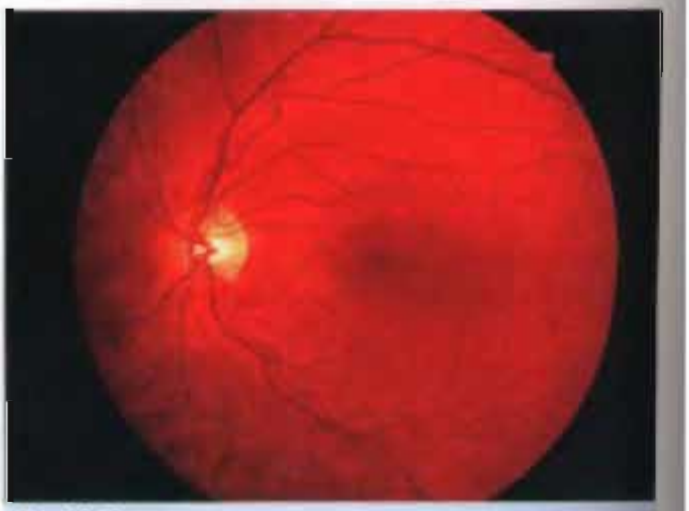

Fig. 11.43
Diffuse choroidal haemangioma

Metastatic tumours

The choroid is by far the most common site for uveal metastases, accounting for about 90%, followed by the iris and ciliary body. Metastatic tumours to the choroid are more common than primary malignancies but their presence is usually undetected or overshadowed by the patient's general illness. The most frequent primary site is the breast in women and the bronchus in both sexes. A choroidal secondary may be the initial presentation of a bronchial carcinoma, whereas a past history of breast cancer is the rule in patients with breast secondaries. Other less common primary sites include the gastrointestinal tract, kidney and skin melanoma. The prostate is, however, an extremely rare primary site. Patient survival is generally poor, with a median of 8–12 months for all patients and 15–17 months for those with breast carcinoma. In patients with breast carcinoma risk factors for choroidal metastases include dissemination of disease in more than one organ and the presence of lung and brain metastases.

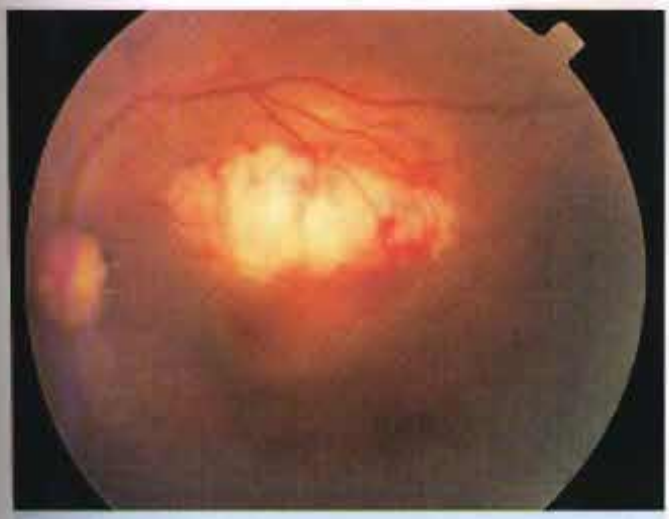

Fig. 11.44
Choroidal metastasis from colon carcinoma (Courtesy of S. Milewski)

Fig. 11.46
Ultrasonogram of choroidal metastasis (*see text*) (Courtesy of M. Karolczak-Kulesza)

Clinical features

1. **Presentation** is usually with visual impairment although metastases may be asymptomatic if located away from the macula.
2. **Signs**
   - A fast-growing, creamy-white, placoid or oval lesion most frequently located at the posterior pole (Fig. 11.44).
   - The tumour seldom becomes significantly elevated because it infiltrates laterally (Fig. 11.45).
   - Occasionally the deposits assume a globular shape and may mimic an amelanotic melanoma.
   - The deposits may be multiple and both eyes are involved in 10–30% of cases.
   - Secondary exudative retinal detachment is frequent and may occur in eyes with relatively small deposits.

Special investigations

1. **Ultrasonography** shows diffuse choroidal thickening and moderate internal acoustic reflectivity (Fig. 11.46).
2. **FA** shows early hyperfluorescence (Fig. 11.47b) with diffuse late staining (Fig. 11.47c and d) but in contrast with choroidal melanomas a 'dual circulation' does not occur.

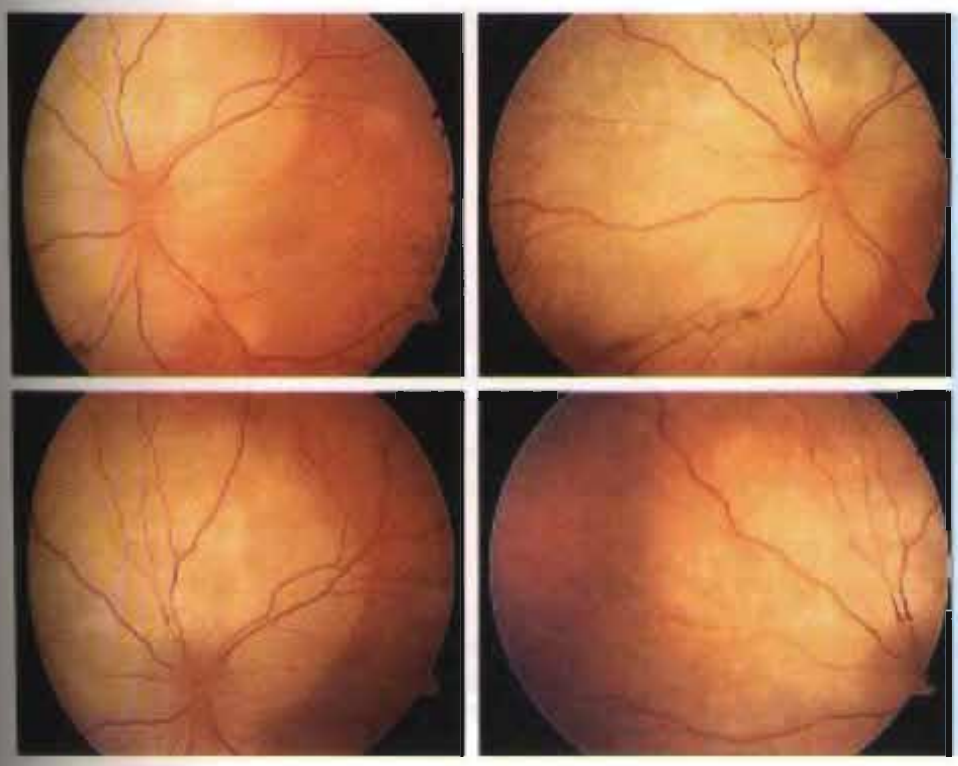

Fig. 11.45
Choroidal metastasis from breast carcinoma (Courtesy of M. Karolczak-Kulesza

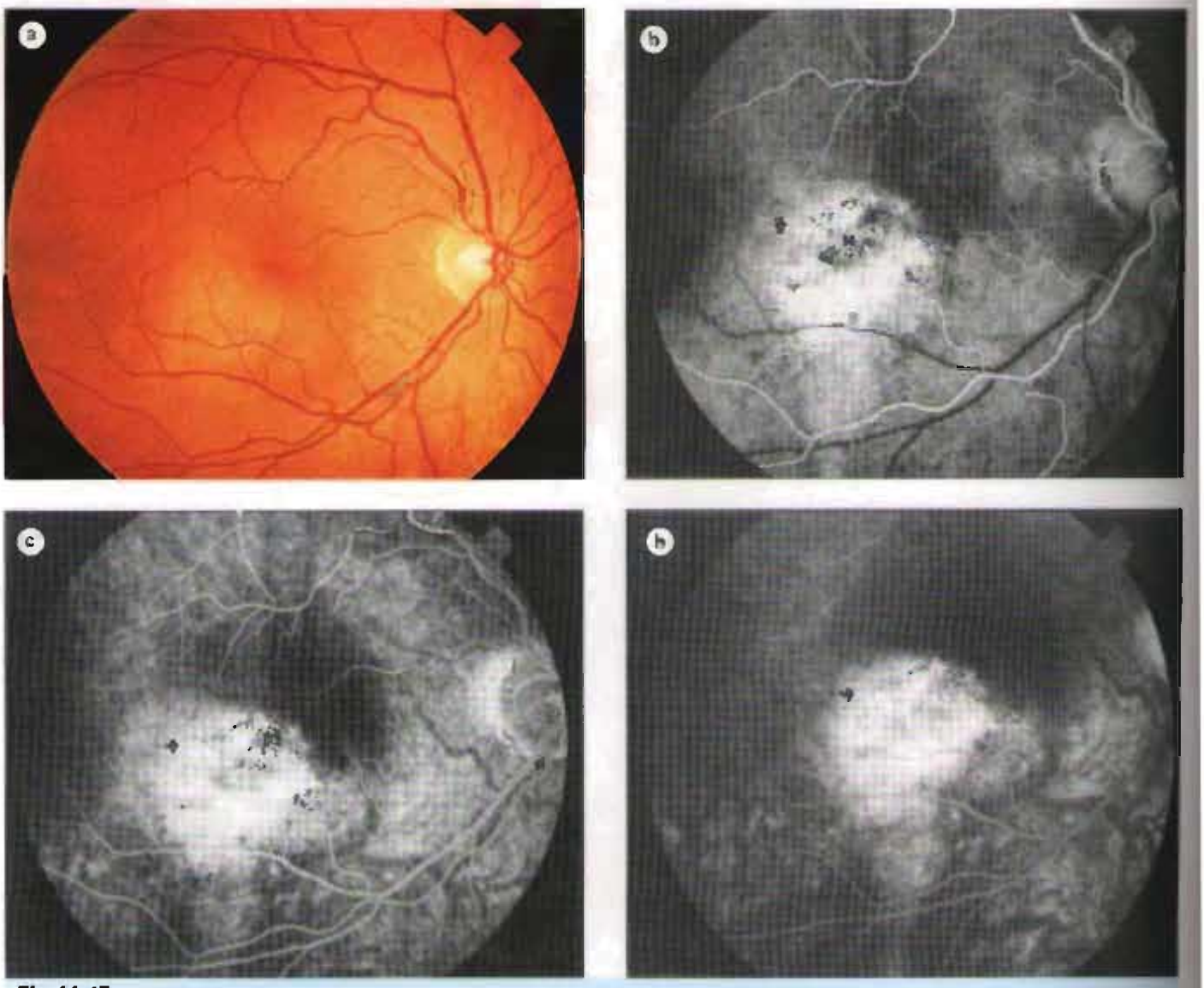

Fig. 11.47
(a) Choroidal metastasis; (b) FA arterial phase showing hyperfluorescence but absence of a 'dual circulation'; (c, d) late phases showing staining (Courtesy of S. Milewski)

3. **Biopsy**, performed either trans-sclerally or by fine-needle aspiration, may be useful.
4. **Systemic** investigations to detect the primary tumour, if unknown, or other metastatic sites.

Treatment

1. **Observation**, if the patient is asymptomatic or receiving systemic chemotherapy.
2. **Radiotherapy**, either external beam or brachytherapy, for small tumours.
3. **Transpupillary thermotherapy** is useful for deposits of moderate thickness and minimal amount of subretinal fluid.
4. **Systemic therapy** for the primary tumour may be beneficial for choroidal metastases.
5. **Enucleation** may be required for a painful blind eye.

Choroidal osseous choristoma

Choroidal osseous choristoma (osteoma) is a very rare, benign, very slow-growing, ossifying tumour which typically affects healthy young women. Both eyes are affected in about 25% of cases but not usually simultaneously.

1. **Presentation** is in the second to third decades with gradual visual impairment if the macular is involved.
2. **Signs.** An orange-yellow lesion with well-defined scalloped borders, most commonly situated at the posterior pole (Fig. 11.48). The tumour grows very slowly with the development of overlying RPE changes (Fig. 11.49).
3. **Complications.** Secondary choroidal neovascularization is common and responds poorly to laser photocoagulation.
4. **FA** shows a diffuse mottled pattern of hyperfluorescence during the early and late phases.

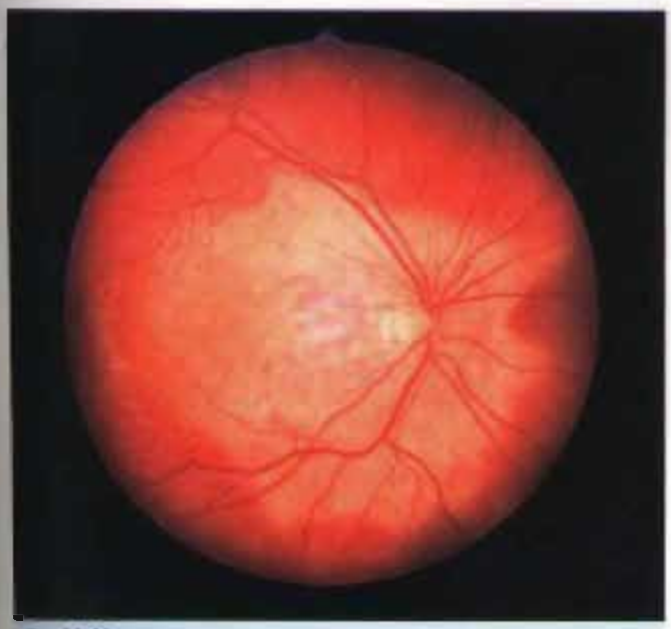

Fig. 11.48
Choroidal osseous choristoma

Fig. 11.49
Same eye several years later showing overlying RPE changes

5. **Ultrasonography** shows a very dense highly reflective lesion (bone) which renders silent the orbital tissue behind it (Fig. 11.50).

Melanocytoma

Melanocytoma is a benign, heavily pigmented tumour that may occur anywhere in the uveal tract, but arises most frequently from dendritic uveal melanocytes in the lamina cribrosa of the optic nerve head. Anterior uveal melanocytomas may undergo acute necrosis with resultant uveitis, pigment dispersion and secondary glaucoma. In contrast with choroidal melanoma, melanocytoma typically affects dark-skinned individuals, although it may also occur in white people.

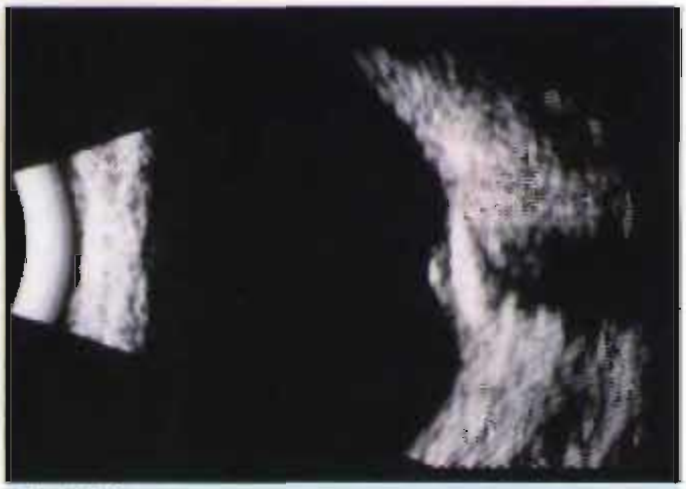

Fig. 11.50
Ultrasonogram of choroidal osseous choristoma (see *text*)

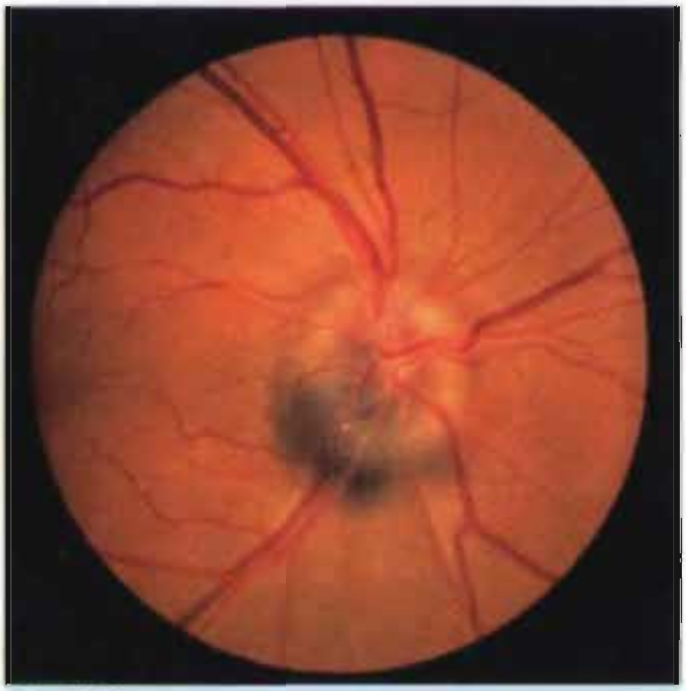

Fig. 11.51
Melanocytoma of the optic nerve head

1. **Presentation** of optic nerve head melanocytoma is usually by chance, although a deep-seated tumour may cause optic nerve dysfunction.
2. **Signs**. A black lesion with feathery edges frequently occupying the inferior part of the disc (Fig. 11.51). Occasionally, the tumour is elevated and occupies the entire disc surface.
3. **Complications**, which are rare, include malignant transformation and central retinal vascular obstruction secondary to spontaneous tumour necrosis.
4. **Treatment** is not required except in the very rare event of malignant transformation.
5. **Differential diagnosis** includes choroidal melanoma invading the optic nerve head and reactive RPE hyperplasia.

Lymphoma

Primary intraocular–central nervous system lymphoma is an uncommon, diffuse, highly malignant, large B-cell (non-Hodgkin) lymphoma. It arises within the brain, spinal cord, leptomeninges and/or the eye and has a poor prognosis, with a 5-year survival rate of less than 33%.

CNS features

1. **At presentation** the following four profiles are seen:
   - Solitary or multiple intracranial nodules.
   - Diffuse meningeal or periventricular lesions.
   - Localized intradural spinal masses.
   - Intraocular involvement.
2. **The diagnosis** is usually made by identifying malignant lymphocytes in the brain, cerebrospinal fluid or vitreous.

Ocular features

Lymphoma tends to involve the vitreous and retina and frequently represents a diagnostic challenge, masquerading as uveitis. Ocular findings usually precede CNS involvement by months or a few years and only 20% of patients have ocular lesions at the time of diagnosis of CNS disease. Both eyes are eventually affected in 80% of cases, but the severity of involvement is often asymmetrical.

1. **Chronic anterior uveitis** unresponsive to steroids.
2. **Intermediate uveitis** in an elderly patient may initially be responsive to steroids but subsequently becomes unresponsive. The vitreous typically shows large clumps or sheets composed of malignant cells.
3. **Posterior segment**
   - Multifocal, large, yellowish, sub-RPE infiltrates are most commonly seen (Fig. 11.52). Coalescence of the lesions may form a ring which is pathognomonic for intraocular lymphoma (Fig. 11.53).
   - Less frequent manifestations include diffuse retinal infiltrates resembling viral retinitis, vascular sheathing and occlusion, and multifocal, tiny deep white lesions which can be misdiagnosed as inflammatory.
4. **Investigations** include neurological evaluation, MRI, lumbar puncture and vitreous biopsy.

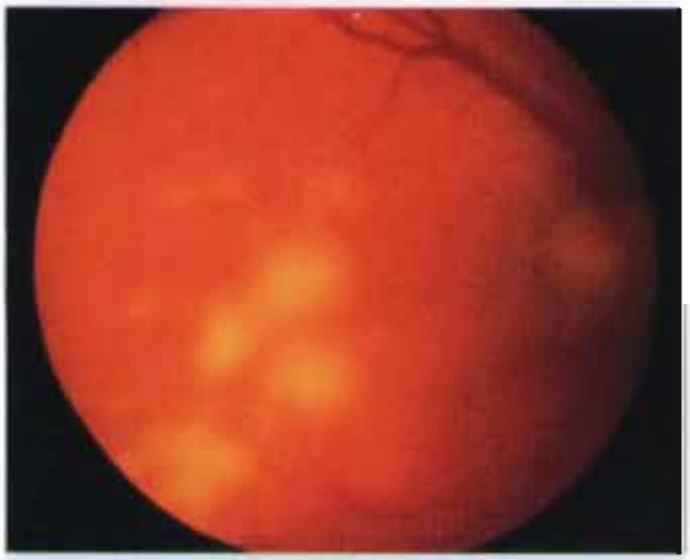

Fig. 11.52
Multifocal lymphomatous subretinal infiltrates (Courtesy of A. Cruess)

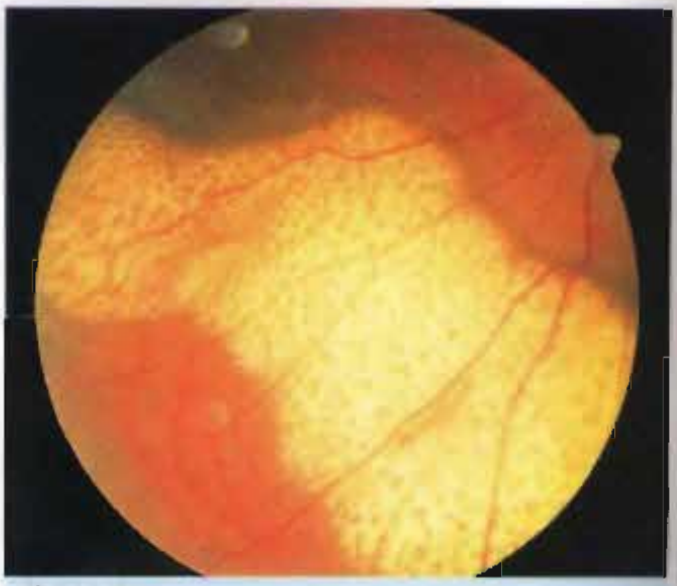

Fig. 11.53
Annular lymphomatous subretinal infiltration (Courtesy of B. Damato)

Treatment

1. **Systemic** treatment is with high-dose external beam radiotherapy to the eyes, sometimes in conjunction with whole brain radiotherapy, and/or systemic or intrathecal chemotherapy.
2. **Intravitreal** methotrexate may be used as primary treatment and for recurrences following systemic therapy.

Retinal and optic nerve head tumours

Retinoblastoma

Retinoblastoma is the most common primary intraocular malignancy of childhood. Even so, it is rare, occurring in about 1:20,000 live births and accounts for about 3% of all childhood cancers.

Genetics

Retinoblastoma results from malignant transformation of primitive retinal cells before final differentiation. Because these cells disappear within the first few years of life, the tumour is seldom seen after 3 years of age. Retinoblastoma

may be heritable or non-heritable. The predisposing gene (*RPE1*) is at 13q14.

1. **Heritable** (germline) retinoblastoma accounts for 40%. In these patients one allele of the *RPE1* (a tumour supressor gene) has mutated in all body cells. When a further mutogenic event ('second hit') affects the second allele, the cell undergoes malignant transformation. Because all the retinal precursor cells contain the initial mutation, these children develop bilateral and multifocal tumours. Familial cases also carry a predisposition to non-ocular cancers; most notably pinealoblastoma (trilateral retinoblastoma) and osteosarcoma. The risk of second malignancy increases greatly if external beam irradiation has been used to treat the original tumour, and the second tumour tends to arise within the irradiated field.
   - The risk of transmitting the gene mutation is 50%, and because of high penetrance 40% of offspring of a survivor of heritable retinoblastoma will develop the tumour.
   - Unaffected parents of a child with bilateral retinoblastoma with no family history have a 40% chance of producing another affected child.
   - Some familial cases present with initially unilateral disease and about 15% of patients with heritable retinoblastoma only express unilateral involvement.
2. **Non-heritable** (somatic) retinoblastoma accounts for 60% of cases. The tumour is unilateral, not transmissible and does not predispose the patient to an increased risk of second non-ocular cancers. Eighty-five per cent of patients with unilateral retinoblastoma fall into this category.

Presentation

The vast majority present within the first 2 years of life. Children with bilateral tumours tend to present earlier (average 12 months) than those with unilateral involvement.

1. **Leukocoria** (white pupillary reflex) is the commonest (60%) (Fig. 11.54).
2. **Strabismus** is the second most common (20%). Fundus examination is therefore mandatory in all cases of childhood strabismus.

Fig. 11.54
Left leukocoria due to advanced retinoblastoma (Courtesy of C. Bary)

Fig. 11.55
Multiple iris nodules due to invasion by retinoblastoma

Fig. 11.56
Pseudo-hypopyon due to anterior segment invasion by retinoblastoma

3. **Secondary glaucoma**, sometimes associated with buphthalmos, is uncommon.
4. **Unilateral iris invasion** in older children (average age 6 years) may manifest as multifocal nodules (Fig. 11.55), resembling granulomatous inflammation, or pseudohypopyon (masquerade syndrome) (Fig. 11.56). It is therefore important to consider retinoblastoma in the differential diagnosis of unusual chronic uveitis in children.
5. **Orbital inflammation** mimicking orbital or preseptal cellulitis may occur with necrotic tumours (Fig. 11.57). It does not necessarily imply extraocular extension and the exact mechanism is not known.
6. **Orbital invasion** may occur in neglected cases (Fig. 11.58).
7. **Metastatic disease** involving regional lymph nodes and brain before the detection of ocular involvement is rare.
8. **Raised intracranial pressure** due to 'trilateral retinoblastoma' before the diagnosis of ocular involvement is very rare.
9. **On routine examination** of a patient known to be at risk.

Fig. 11.57
Orbital inflammation associated with retinoblastoma

Fig. 11.58
Orbital invasion by neglected retinoblastoma

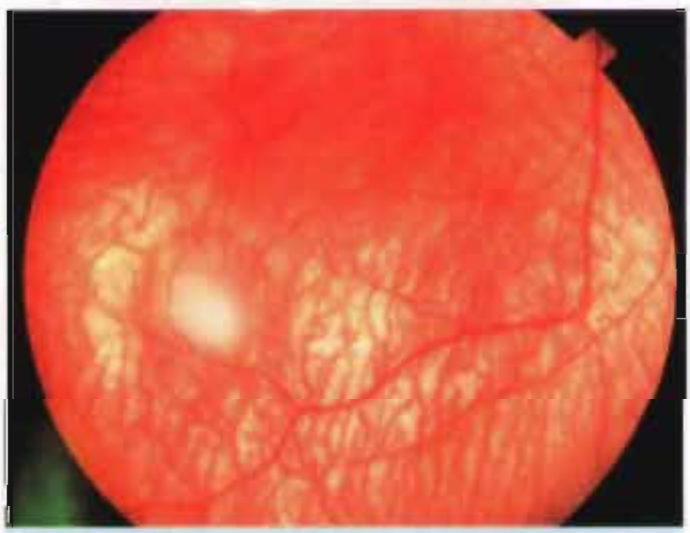

Fig. 11.59
Small intraretinal retinoblastoma

Fig. 11.60
Retinoblastoma

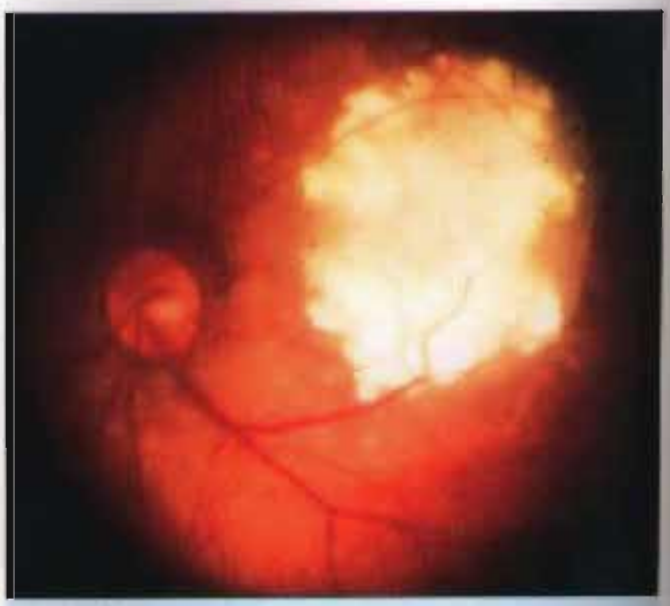

Fig. 11.61
Endophytic retinoblastoma (Courtesy of C. Barry)

Signs

Indirect ophthalmoscopy with scleral indentation must be performed on *both eyes* after full mydriasis. This is because without indentation pre-equatorial tumours may be missed and one eye may harbour multiple tumours. The clinical signs depend on tumour size and growth pattern.

1. **An early intraretinal** tumour is a placoid white lesion (Figs 11.59 and 11.60).
2. **An endophytic** tumour grows inwards towards the vitreous, projecting from the retinal surface as a white, cottage cheese-like mass, with surface blood vessels (Fig. 11.61).
3. **An exophytic** tumour grows outwards as a subretinal, multilobulated white mass (Fig. 11.62). It detaches the retina and may be difficult to visualize if the subretinal fluid is deep (Fig. 11.63).

Fig. 11.62
Exophytic retinoblastoma (Courtesy of S. Milewski)

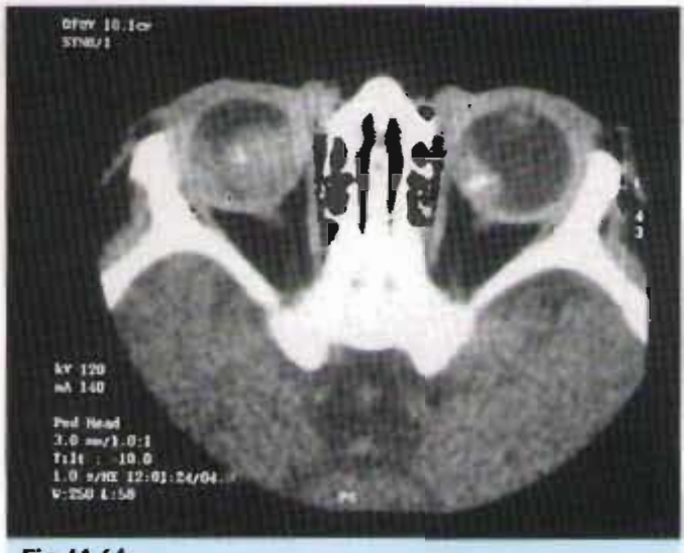

Fig. 11.64
CT scan showing bilateral advanced retinoblastomas (Courtesy of K. Nischal)

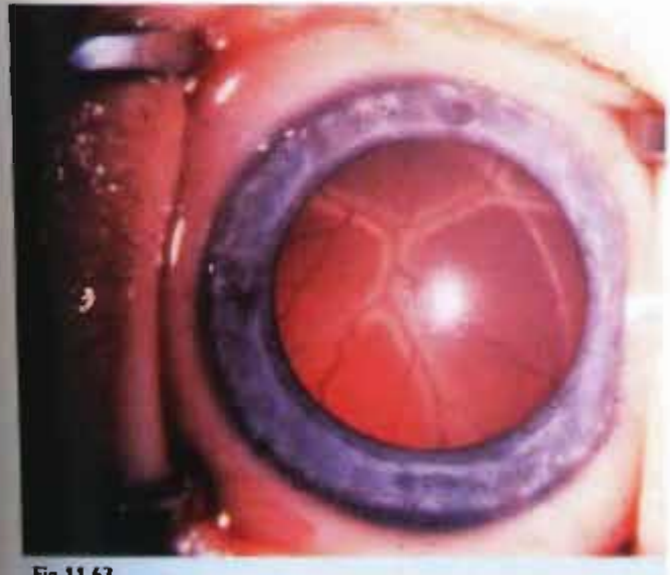

Fig. 11.63
Retinal detachment caused by exophytic retinoblastoma

Special investigations

1. **Ultrasonography** is used mainly to assess tumour size. It also detects calcification within the tumour and is helpful in the diagnosis of simulating lesions such as Coats disease and toxocariasis.
2. **CT** demonstrates gross involvement of the optic nerve, orbital and CNS extension, and the presence of pinealoblastoma and calcification (Fig. 11.64). However, it entails a significant dose of radiation which may be dangerous in patients with germinal mutations.
3. **MRI** cannot detect calcification, but is superior to CT for optic nerve evaluation and detection of a pinealoblastoma, especially when contrast is used. MRI may also be useful to differentiate retinoblastoma from simulating conditions.
4. **Systemic investigations** such as bone marrow aspiration and lumbar puncture are performed only in patients with optic nerve involvement or evidence of extraocular extension.

Treatment

Treatment is related to tumour size, location and associated findings such as retinal detachment, subretinal and vitreous tumour seeds and the state of the fellow eye.

1. **Small tumours**, no more than 4 mm diameter and 2 mm thickness without vitreous or subretinal seeds can be treated with transpupillary thermotherapy laser or cryo-

Fig. 11.65
Small peripheral retinoblastoma seen on scleral indentation

therapy. The latter is particularly useful for pre-equatorial tumours which are difficult to reach with laser (Fig. 11.65).

2. **Medium-size tumours**
   a. ***Brachytherapy*** is indicated for tumours of no more than 12 mm diameter and 6 mm thickness, which are unsuitable for thermotherapy or cryotherapy, provided there is no vitreous seeding. Following treatment the tumour regresses leaving a calcific residue (Fig. 11.66).
   b. ***Chemotherapy*** with carboplatin, vincristine and etoposide which may be combined with cyclosporin. The drugs are given intravenously in 3 week cycles over a 4–9 month period depending on disease severity. This may be followed by local treatment with cryotherapy or thermotherapy to consolidate tumour control.

Fig. 11.66
Regressed retinoblastoma with calcific residue

Fig. 11.67
Large retinoblastoma with new surface vessels

   c. ***External beam radiotherapy*** should be avoided, if possible, due to the high risk of complications such as cataract formation, radiation retinopathy and cosmetic deformities. In patients with germinal mutations there is also a risk of inducing a second malignancy such as sarcoma of bone or connective tissue.
3. **Large tumours** (Fig. 11.67)
   a. ***Chemotherapy*** to shrink the tumour (chemoreduction), facilitating subsequent local treatment, thereby avoiding enucleation or external beam radiotherapy. Chemotherapy also will have a beneficial effect if a smaller tumour is present in the fellow eye.
   b. ***Enucleation*** if chemoreduction fails or a normal fellow eye makes aggressive chemotherapy inappropriate. It is also useful for diffuse retinoblastoma because of poor visual prognosis and high risk of recurrence with other therapeutic modalities. Enucleation should be performed with minimal manipulation and it is imperative to obtain a long piece of optic nerve (8–12 mm). There is no contraindication to the insertion of an orbital implant. Unfortunately subsequent shortening of the fornices and retraction of the implant (post-enucleation socket syndrome) may require further surgical intervention.
4. **Extraocular extension** beyond the lamina cribrosa is treated with chemotherapy after enucleation. Extension to the cut end of the optic nerve, or extension through the sclera, is treated with chemotherapy and irradiation of the affected orbit.
5. **Metastatic disease** is treated with high-dose chemotherapy. Patients with malignant cells in the cerebrospinal fluid may require intrathecal methotrexate.

Prognostic factors

The overall mortality rate is 2–5% and is related to the following:

1. **Tumour size and location.** Small posterior tumours do best but there is no significant difference between endophytic and exophytic types.

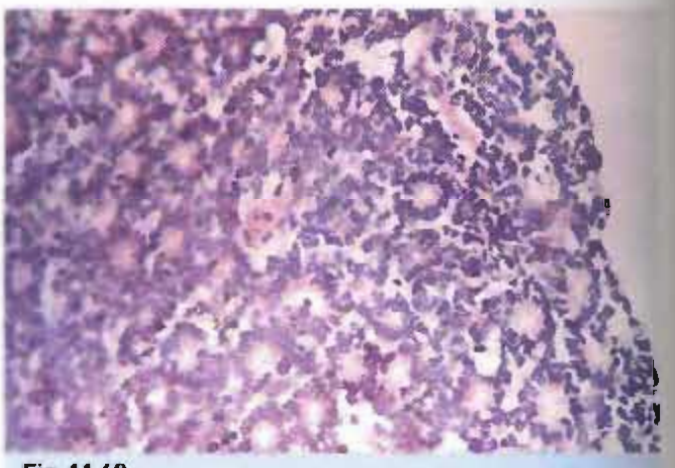

Fig. 11.68
Well-differentiated retinoblastoma with abundant rosettes
(Courtesy of A. Garner)

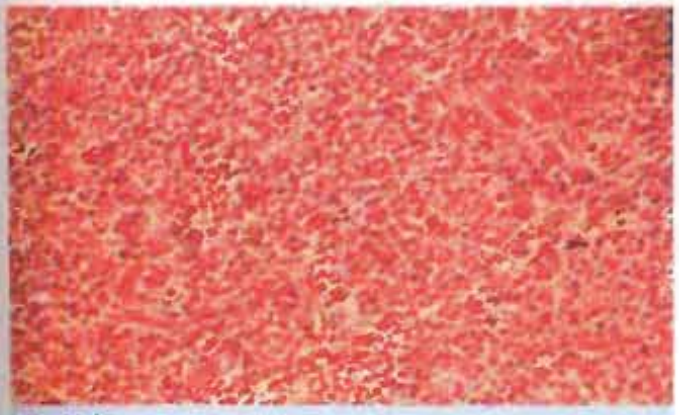

Fig. 11.69
Highly undifferentiated retinoblastoma (Courtesy of A. Garner)

Fig. 11.71
Persistent hyperplastic primary vitreous

Fig. 11.70
Leukocoria associated with persistent hyperplastic primary vitreous

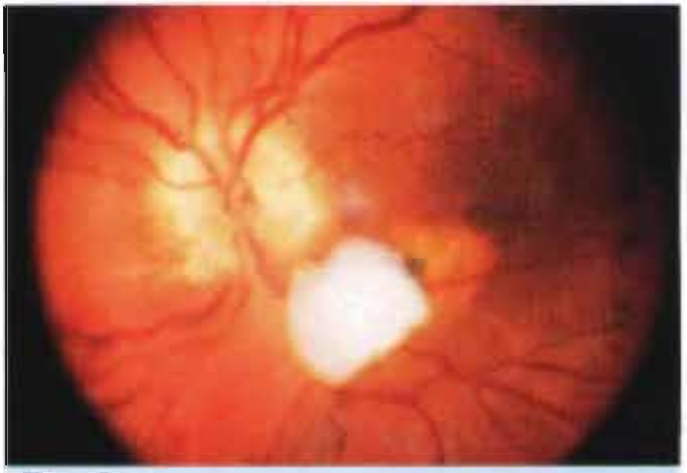

Fig. 11.72
Toxocara granuloma resembling endophytic retinoblastoma

2. **Cellular differentiation.** The mortality rate of patients whose tumours have abundant rosettes (Fig. 11.68) is much less than in those with highly undifferentiated tumours (Fig. 11.69).
3. **Optic nerve involvement** beyond the point of surgical transection is associated with high mortality.
4. **Invasion** of the choroid or vortex veins facilitates haematogenous spread and is therefore of adverse prognostic significance.
5. **Extrascleral spread** carries a grave prognosis.

Differential diagnosis

1. **Persistent hyperplastic primary vitreous** is an important cause of congenital leukocoria (Fig. 11.70). It typically occurs in a microphthalmic eye and is almost always unilateral. It is characterized by a retrolental mass into which elongated ciliary processes are inserted (Fig. 11.71). With time the mass contracts and pulls the ciliary processes centrally so that they become visible through the pupil. An associated dehiscence involving the posterior capsule may lead to subsequent cataract formation.
2. **Coats disease** is almost always unilateral, more common in boys and tends to present later than retinoblastoma. It is characterized by telangiectatic retinal blood vessels, extensive intra- and subretinal yellow exudation and exudative retinal detachment (*see* Chapter 14).
3. **Retinopathy of prematurity**, if advanced, may cause retinal detachment and leukocoria. Diagnosis is usually straightforward because of the history of prematurity and low birth weight (*see* Chapter 14).
4. **Toxocariasis** (*see* Chapter 10).
   a. ***Chronic toxocara endophthalmitis*** may cause a cyclitic membrane and a white pupil.
   b. ***Toxocara granuloma*** at the posterior pole may resemble an endophytic retinoblastoma (Fig. 11.72).
5. **Intermediate uveitis** may mimic the diffuse infiltrating type of retinoblastoma seen in older children (*see* Chapter 10).
6. **Retinal dysplasia** is characterized by a congenital pink or white retrolental membrane in a microphthalmic eye, with a shallow anterior chamber and elongated ciliary processes. Unilateral cases are usually not associated with systemic abnormalities. Patients with bilateral involvement may

Fig. 11.73
Vesiculobullous dermatitis in incontinentia pigmenti

Fig. 11.74
Cicatricial retinal detachment in incontinentia pigmenti

have Norrie disease or Warburg, Patau and Edward syndromes.

7. **Incontinentia pigmenti** (Bloch–Sulzberger syndrome) is a rare X-linked dominant disorder affecting girls. It is characterized by vesiculobullous dermatitis (Fig. 11.73) on the trunk and extremities. Malformations of teeth, hair, nails, bones and central nervous system may also be present. About one-third of children develop cicatricial retinal detachment which may cause leukocoria in the first year of life (Fig. 11.74).
8. **Retinocytoma** (retinoma) is thought to be a benign variant of retinoblastoma. It is characterized by calcified mass associated with RPE alteration and chorioretinal atrophy (Fig. 11.75). The appearance is remarkably similar to that of a retinoblastoma following irradiation (*see* Fig. 11.66).
9. **Retinal astrocytoma** (*see* below).

Retinal astrocytoma

Astrocytoma of the retina or optic nerve head is a rare, benign, non-vision-threatening tumour. It may occur in

Fig. 11.75
Retinocytoma (Courtesy of K. Nischal)

Fig. 11.76
Nodular retinal astrocytoma

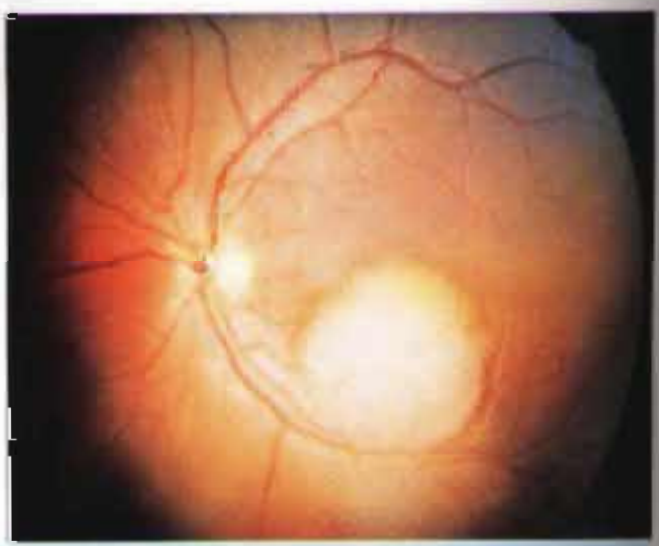

Fig. 11.77
Flat retinal astrocytoma (Courtesy of C. Barry)

isolation but is most frequently seen in patients with tuberous sclerosis (*see* Chapter 20). About 50% of patients with tuberous sclerosis have fundus astrocytomas, which may be multiple and are bilateral in about 15% of cases.

Signs

- A semi-translucent nodule (Fig. 11.76) or a white, relatively flat, well-circumscribed plaque (Fig. 11.77).
- Later, the tumour becomes more solid and white and may, on cursory examination, resemble retinoblastoma (Fig. 11.78).
- Multiple areas of calcification within a long-standing tumour may give rise to a fossilized, mulberry-like appearance (Fig. 11.79).

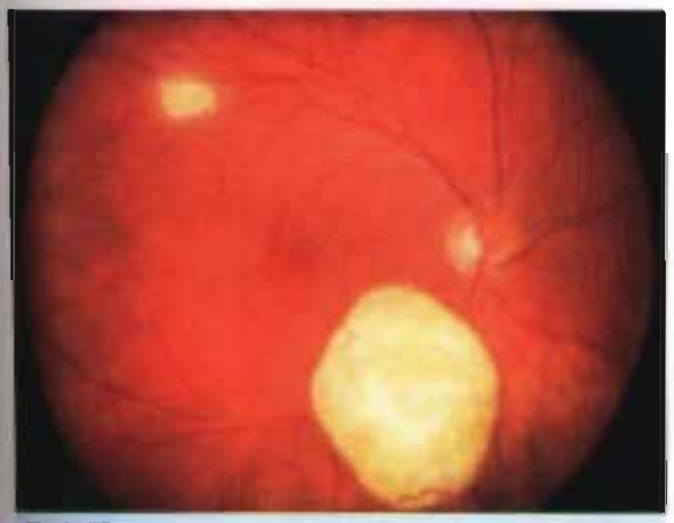

Fig. 11.78
Long-standing retinal astrocytomas

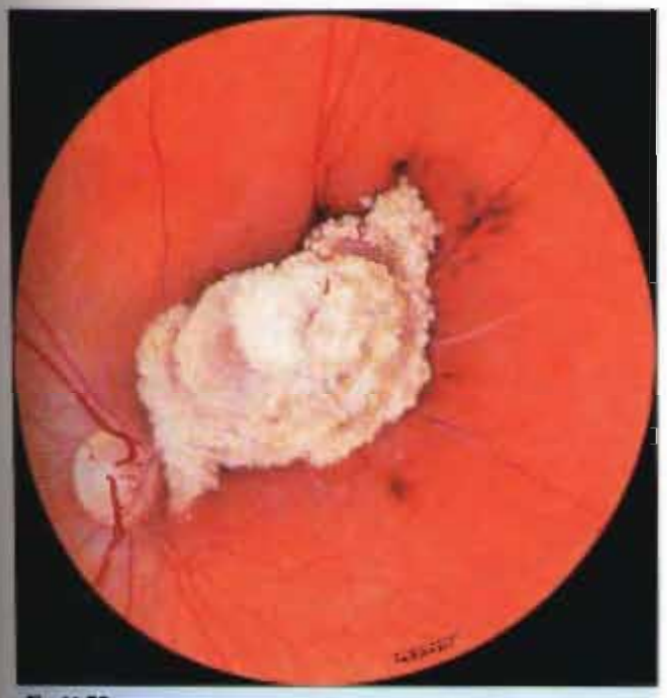

Fig. 11.79
Calcified mulberry-like retinal astrocytoma

Retinal capillary haemangioma

Capillary haemangioma of the retina or optic nerve head is a rare, sight-threatening vascular hamartoma which may occur in isolation (von Hippel disease). However about 50% of patients with solitary capillary haemangiomas and virtually all patients with multiple lesions have systemic disease. The combination of systemic and ocular lesions is referred to as the von Hippel–Lindau syndrome (V-H-L) (*see* Chapter 20). The prevalence of retinal capillary haemangiomas in patients with V-H-L is approximately 60%.

Endophytic

1. **Presentation** is in the second to third decades with unilateral or bilateral ocular involvement on screening, or with visual impairment.
2. **Signs** (in chronological order)
   - A tiny red lesion located within the capillary bed between an arteriole and a venule (Fig. 11.80).

Fig. 11.80
Early retinal capillary haemangioma

Fig. 11.81
Retinal capillary haemangioma (Courtesy of S. Milewski)

- A small, well-defined nodule (Fig. 11.81).
- A round orange-red mass associated with dilatation and tortuosity of the supplying artery and draining vein due to arteriovenous shunting so that both vessels appear similar (Fig. 11.82).

3. **FA** shows early hyperfluorescence (Fig. 11.83a) and late leakage (Fig. 11.83b).
4. **Complications** include hard exudate formation in the area surrounding the tumour and/or at the macula (*see* Fig. 11.85), macular oedema, epiretinal membrane formation, retinal detachment which may be tractional or exudative, and vitreous haemorrhage

Other types

1. **Exophytic haemangioma** is less common, arises from the outer retina in the juxtapapillary region and presents with visual loss. It is characterized by a sessile, ill-defined lesion with dilated blood vessels, which may be associated with retinal oedema and haemorrhage (Fig. 11.84). It carries a high risk of exudative retinal detachment.
2. **Optic nerve head haemangioma** (Fig. 11.85)

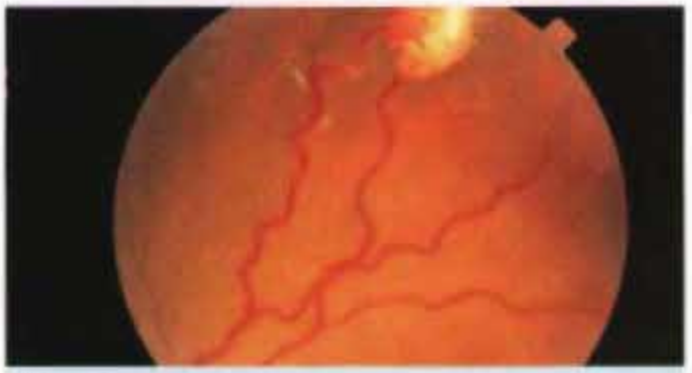

Fig. 11.82
Vascular dilatation and tortuosity associated with a retinal capillary haemangioma

Fig. 11.84
Exophytic retinal capillary haemangioma (Courtesy of S. Milewski)

Treatment

1. **Argon laser photocoagulation** for small peripheral lesions (Fig. 11.86a). Following successful treatment the calibre of the feeding blood vessels returns to normal (Fig. 11.86b).
2. **Cryotherapy** for larger peripheral lesions or those with exudative retinal detachment. Vigorous treatment of a large lesion may cause a temporary but extensive exudative retinal detachment.
3. **Brachytherapy** for lesions one to two disc diameters in size.
4. **Vitreoretinal surgery** may be required for non-absorbing vitreous haemorrhage, epiretinal fibrosis or tractional retinal detachment. If appropriate, the tumour may be destroyed by endolaser photocoagulation.

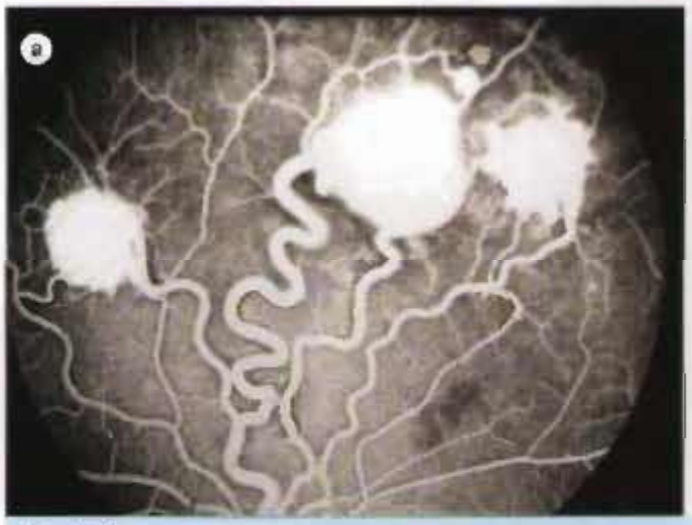

Fig. 11.83
(a) Early FA of multiple retinal capillary haemangiomas showing hyperfluorescence due to filling; (b) late phase showing leakage (Courtesy of S. Milewski)

Screening

Because it is impossible to predict which patients with retinal angiomas will also harbour systemic lesions, the ophthalmologist must refer all such patients for systemic and neurological evaluation. Relatives should also be screened because of the dominant inheritance pattern of the disease. Apart from physical examination, the following screening protocol should be regularly performed in patients with established V-H-L and relatives at risk:

1. **Annual screening**
   - Eye examination, physical examination and blood pressure measurement.
   - Renal ultrasonography from age 16 years.
   - Twenty-four hour urine collection for estimation of vanillyl mandelic acid and catecholamine levels from age 10 years to detect phaeochromocytoma.
2. **Screening every 3 years** involves abdominal and brain MRI scans from age 15 years.

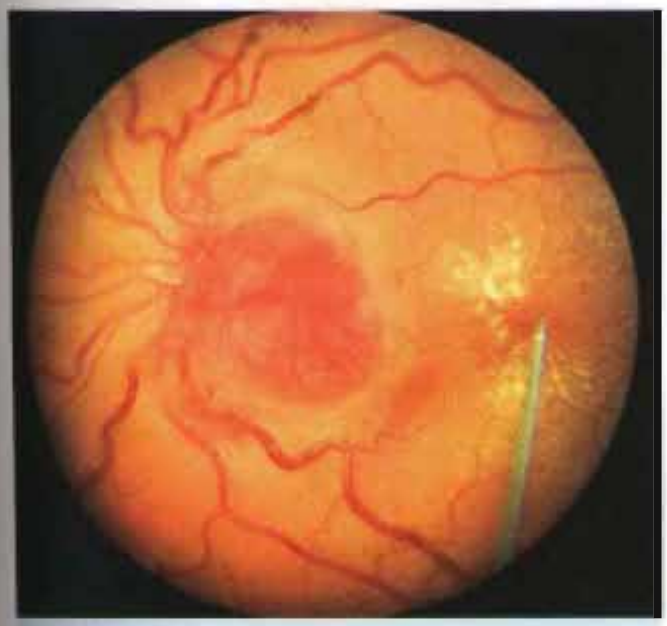

Fig. 11.85
Capillary haemangioma of the optic nerve head with macular exudates (Courtesy of K. Nischal)

Retinal cavernous haemangioma

Cavernous haemangioma of the retina or optic nerve head is a rare, congenital, unilateral, vascular hamartoma. A minority of patients have similar lesions of the skin and CNS. The combination is inherited in autosomal dominant fashion and is referred to as *neuro-oculocutaneous phaconuatosis* or alternatively as *cavernoma multiplex*.

1. **Presentation** is in the second to third decades with vitreous haemorrhage, or more often as a chance finding.
2. **Signs** vary from a collection of aneurysms (Fig. 11.87) to an elaborate complex of vascular anomalies on the retina (Fig. 11.88) or optic nerve head (Fig. 11.89) which may rarely bleed (Fig. 11.90). Because of sluggish flow of blood, the red cells may sediment and separate from plasma, giving rise to 'menisci', or fluid levels within the lesion.
3. **Treatment** is generally not required although vitrectomy may be necessary in the rare event of non-absorbing vitreous haemorrhage.

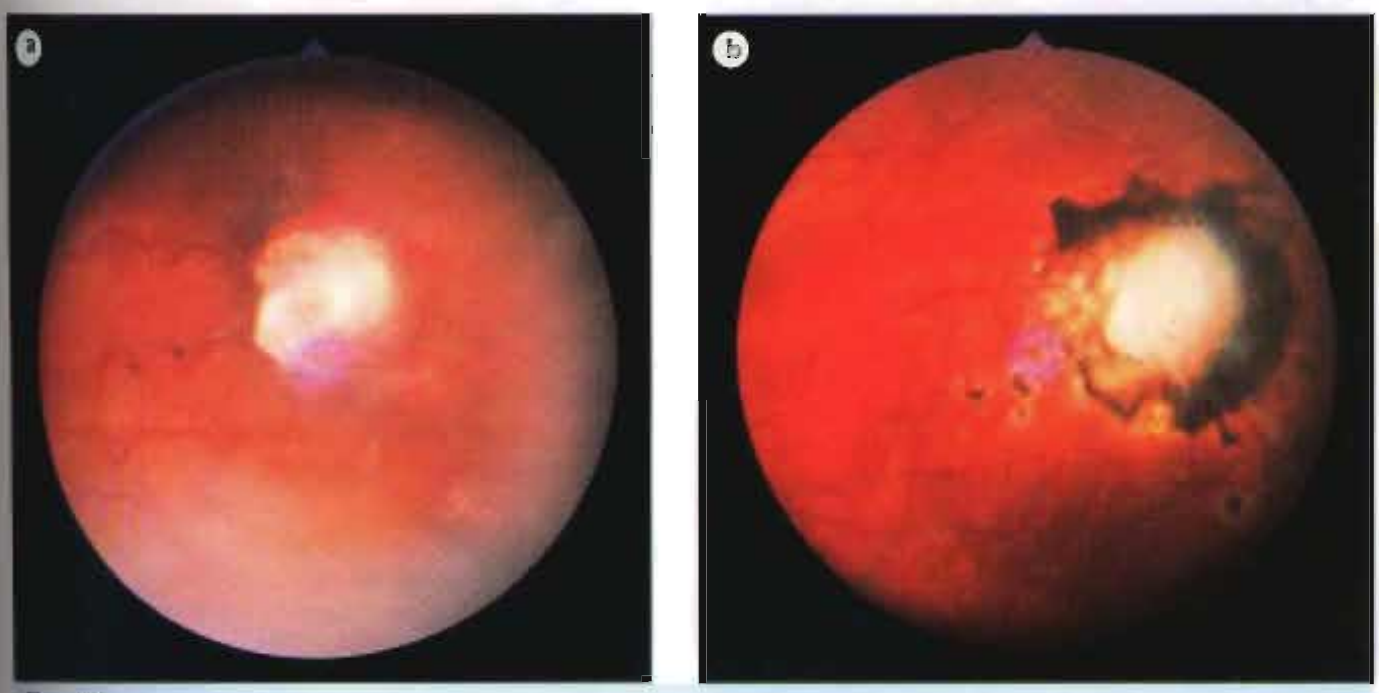

Fig. 11.86
(a) Retinal capillary haemangioma; (b) following laser photocoagulation

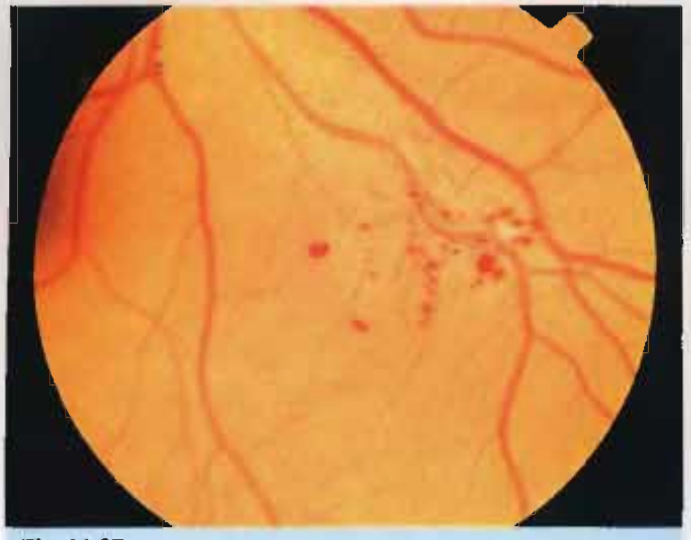

Fig. 11.87
Small retinal cavernous haemangioma (Courtesy of S. Milewski)

Fig. 11.90
Haemorrhage from retinal cavernous haemangioma

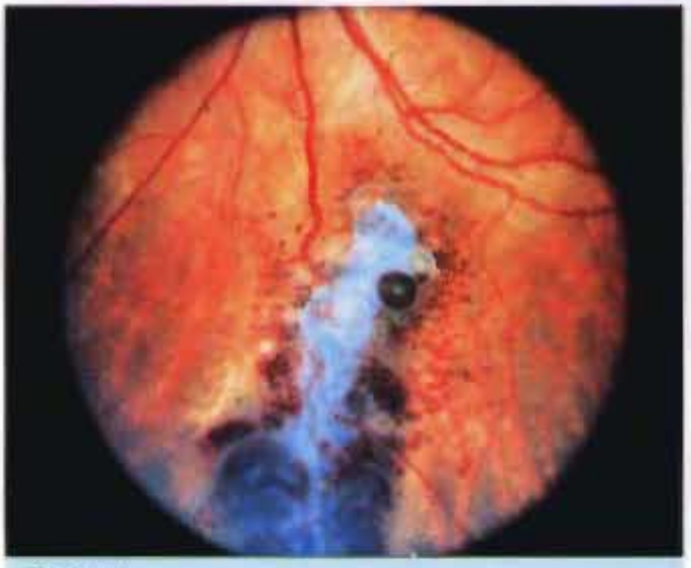

Fig. 11.88
Retinal cavernous haemangioma

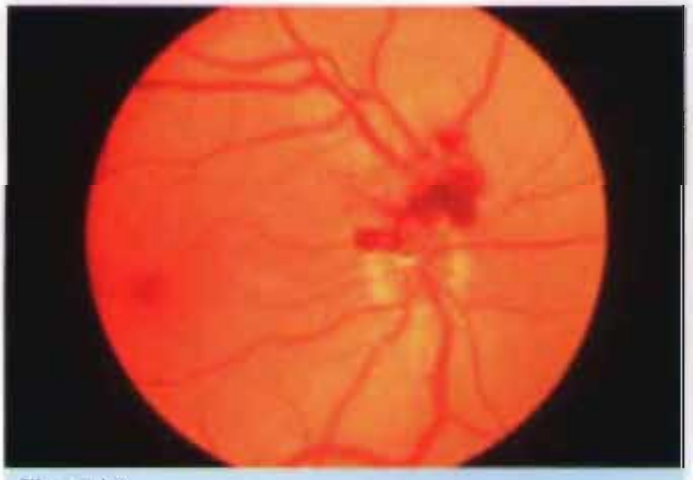

Fig. 11.89
Cavernous haemangioma of the optic nerve head (Courtesy of P. Morse)

Retinal racemose haemangioma

Racemose haemangioma of the retina and optic nerve head is a rare, usually unilateral, congenital arteriovenous malformation involving direct communication between the arteries and veins without an intervening capillary bed. Some patients have similar ipsilateral lesions involving the midbrain, basofrontal region and posterior fossa, an association which is referred to as the *Wyburn–Mason syndrome*. Brain involvement may lead to spontaneous haemorrhage or epilepsy. Occasionally, malformations may involve the maxilla, mandible and orbit. Facial skin lesions have also been reported.

1. **Presentation** may be with visual impairment or more commonly as a chance finding.
2. **Signs**. Enlarged, tortuous blood vessels which are often more numerous than in a normal fundus, with the vein and artery appearing similar (Fig. 11.91a).
3. **FA** shows absence of leakage (Fig. 11.91b–d) but very large lesions may occasionally lead to exudation and haemorrhage.
4. **Treatment** is not required.

Retinal vascular proliferative tumour

Retinal vasoproliferative tumour is a rare gliovascular lesion which occurs mostly in healthy individuals. It can be mistaken for a variety of other entities, most notably retinal angiomas, amelanotic choroidal melanomas and retinal telangiectasia.

1. **Presentation** is in the fifth to sixth decades with blurring of vision due to macular exudation.
2. **Signs**. A solitary, highly vascularized, yellow, retinal or subretinal mass with normal feeding and draining vessels (Fig. 11.92).
3. **Complications** include haemorrhage, exudation, cystoid macular oedema, epiretinal fibrosis and exudative retinal detachment.

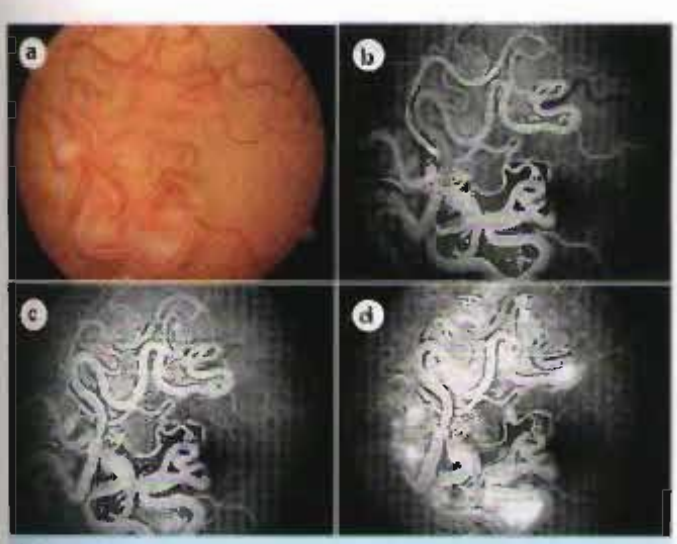

Fig. 11.91
(a) Retinal racemose haemangioma; (b–d) FA showing filling but no leakage (Courtesy of M. Karolczak-Kulesza)

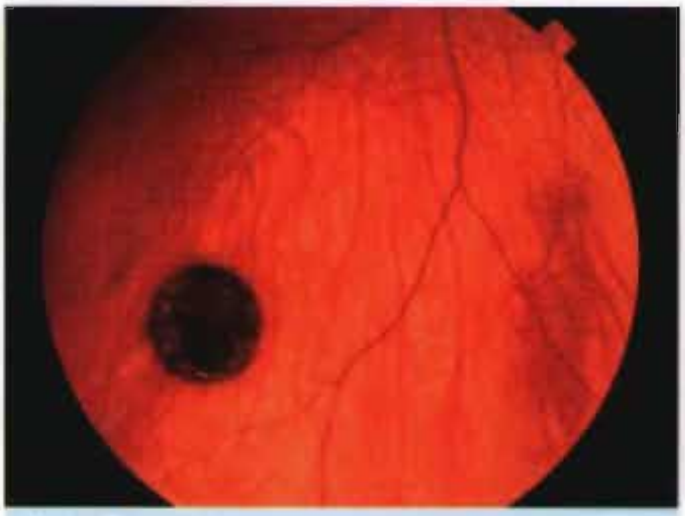

Fig. 11.93
Typical solitary congenital RPE hypertrophy with peripheral depigmentation

Fig. 11.92
Retinal vascular proliferative tumour (Courtesy of B. Damato)

Fig. 11.94
Typical solitary congenital RPE hypertrophy with hypopigmented central lacunae

4. **Treatment** with cryotherapy, laser photocoagulation or brachytherapy may be beneficial but the visual prognosis is guarded.

Tumours of the retinal pigment epithelium

Congenital hypertrophy of the retinal pigment epithelium

Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is a common benign lesion that may be (a) *typical*, which may be solitary or grouped, or (b) *atypical*. It is important to differentiate the two types because the latter has important systemic implications.

Typical CHRPE

1. Solitary

- A unilateral, flat, dark-grey or black, well-demarcated, round or oval lesion one to three disc diameters in size frequently with a hypopigmented rim just within the outer margin (Fig. 11.93).
- Depigmented lacunae which often enlarge or coalesce may be observed, particularly in older patients (Fig. 11.94).
- Some lesions may become depigmented with only a thin rim of residual pigment remaining at the margin (Fig. 11.95).

2. Grouped

- Usually unilateral, variably sized, sharply circumscribed, round, oval dark-grey or black lesions, often organized in a pattern simulating animal footprints (bear-track pigmentation) (Fig. 11.96).

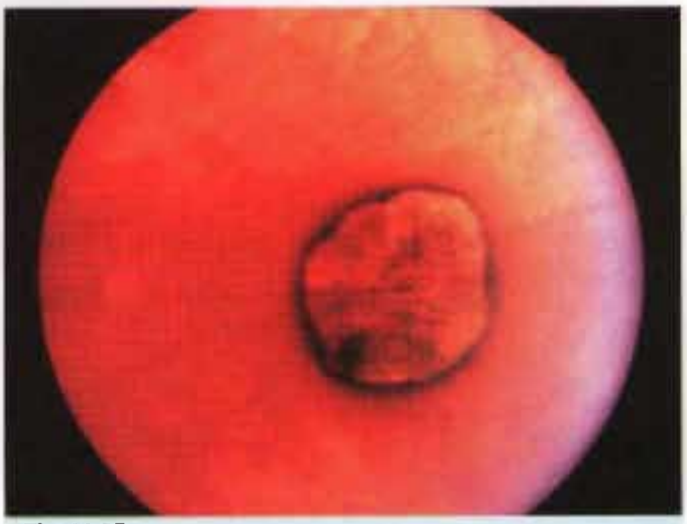

Fig. 11.95
Typical solitary congenital RPE hypertrophy which is nearly completely hypopigmented apart from a peripheral ring

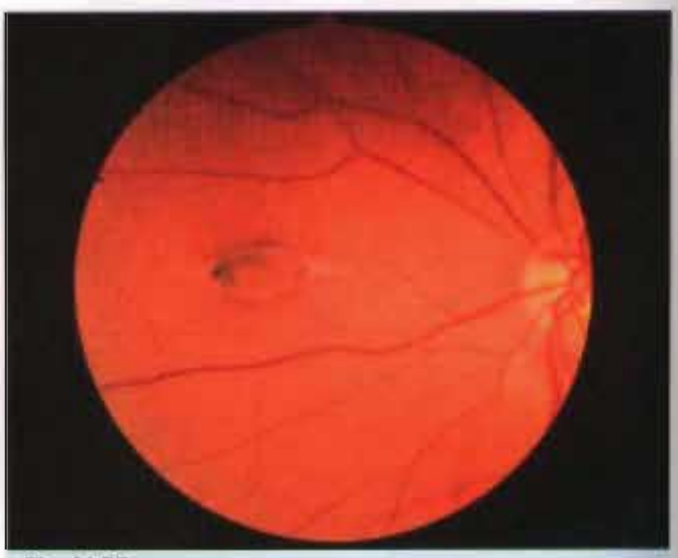

Fig. 11.97
Atypical congenital RPE hypertrophy (Courtesy of B. Jay)

Fig. 11.96
Typical grouped congenital RPE hypertrophy

Fig. 11.98
Intestinal adenomatous polyposis

- The lesions are often confined to one sector or quadrant of the fundus, with the smaller spots usually located more centrally.

Atypical CHRPE

1. Signs

- Multiple, bilateral, widely separated, frequently oval or spindle-shaped lesions of variable size associated with hypopigmentation at one margin (Fig. 11.97).
- The lesions have a haphazard distribution and may be pigmented, depigmented or heterogenous.

2. Systemic implications

*a. **Familial adenomatous polyposis*** (FAP) is a dominantly inherited condition characterized by adenomatous polyps throughout the rectum and colon which usually start to develop in adolescence (Fig. 11.98). If untreated, virtually all patients with FAP develop carcinoma of the colorectal region by the age of 50 years. From the age of 10 years, persons at risk should undergo regular endoscopic examinations and a prophylactic total colectomy should be performed early in adult life in all affected persons. As a result of the dominant inheritance pattern, intensive survey of family members is imperative. The FAP gene has been identified on 5q21–q22. Thus, molecular genetic analysis may identify carriers of the disease in selected cases. Over 80% of patients with FAP have atypical CHRPE which is present at birth. A positive criterion for FAP is the presence of at least four lesions whatever their size, or at least two lesions one of which must be large. Such fundus lesions in a family member should therefore arouse suspicion of FAP.

*b. **Gardner syndrome*** is characterized by FAP, osteomas of the skull and mandible and cutaneous soft tissue tumours such as epidermoid cysts, lipomas and fibromas.

*c. **Turcot syndrome*** is characterized by FAP and tumours of the CNS, particularly medulloblastoma and glioma.

Combined hamartoma of the retinal pigment epithelium and retina

Combined hamartoma of the RPE and retina is a rare, usually unilateral malformation which may be juxtapapillary or peripheral. It predominantly affects males and is found with increased frequency in patients with neurofibromatosis-2.

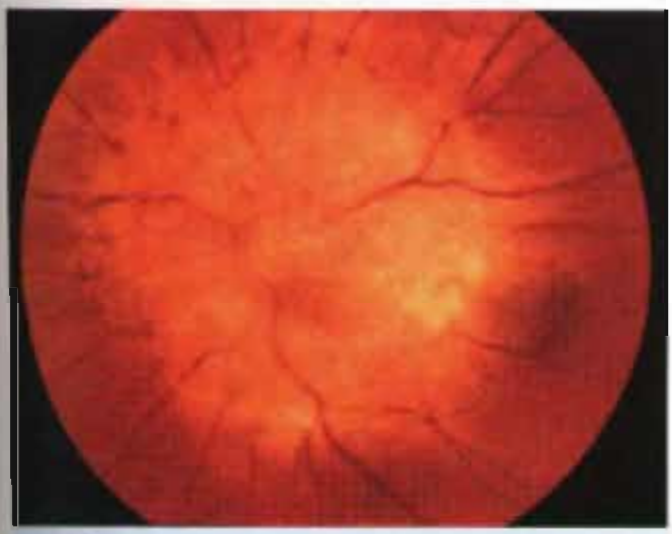

Fig. 11.99
Juxtapapillary combined hamartoma of the RPE and retina

Fig. 11.100
Distortion of the retina by a combined hamartoma of the RPE and retina

1. **Juxtapapillary**
   a. ***Presentation*** is in late childhood or early adulthood with blurred vision and metamorphopsia.
   b. ***Signs***. Deep, slightly elevated, greyish-brown pigmentation associated with variable intra- and epiretinal gliosis, a fine network of dilated capillaries and vascular tortuosity (Fig. 11.99).
2. **Peripheral**
   a. ***Presentation*** is in early childhood with strabismus.
   b. ***Signs***. A linear ridge associated with stretched blood vessels.
3. **Complications** include retinal and/or optic nerve head distortion (Fig. 11.100), macular oedema, choroidal neovascularization and, rarely, retinoschisis and retinal detachment.
4. **Treatment** of epiretinal membranes by vitreoretinal surgery may be tried but the visual results are often disappointing.

Hamartoma of the retinal pigment epithelium

This is an uncommon, small, jet-black lesion involving the RPE, often at the macula, which has a tendency to spill onto the surrounding inner retinal surface (Fig. 11.101).

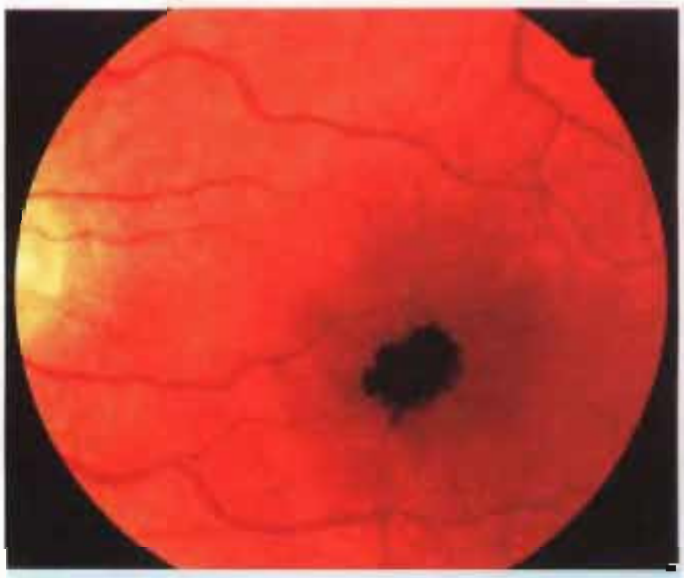

Fig. 11.101
Hamartoma of the RPE

CHAPTER 11

Intraocular Tumours

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Iris tumours

Iris melanoma

In general, uveal melanomas are three times commoner in patients with blue/grey than brown irides. They are extremely rare in black people and there is no sexual predilection. Conditions associated with or predisposed to early-onset uveal melanomas are: (a) *ocular melanocytosis*, (b) *naevus of Ota*, (c) *dysplastic cutaneous naevi*, (d) *familial melanoma* and (e) *neurofibromatosis-1*. Iris melanoma makes up about 5% of uveal melanomas. The majority are composed of spindle B cells (*see* below) and are of low malignancy. A minority contain an epithelioid cell component and can be aggressive. The tumour usually grows very slowly along the iris surface and may invade the angle and anterior ciliary body. The prognosis is very good and only about 5% of patients develop metastases.

Clinical features

1. **Presentation** is in the fifth to sixth decades, a decade earlier than ciliary body and choroidal melanoma, with enlargement of a pre-existing iris lesion.
2. **Signs**
   a. Typical
   - A pigmented or non-pigmented nodule at least 3 mm in diameter and 1 mm thickness located in the *inferior half* of the iris with a smooth or irregular surface (Fig. 11.1). Surface vascularity is also present and is easier to detect in a non-pigmented (Fig. 11.2) than a highly pigmented tumour, where it may be masked.
   - Pupillary distortion, ectropion uveae and occasionally localized cataract may be seen (Fig. 11.3).
   - Features associated with a prominent epithelioid cell component include prominent vascularity, rapid growth and heterogeneous pigmentation.

Fig. 11.2
Non-pigmented iris melanoma with prominent surface vessels

Fig. 11.3
Iris melanoma causing distortion of the pupil, ectropion uveae and a localized lens opacity

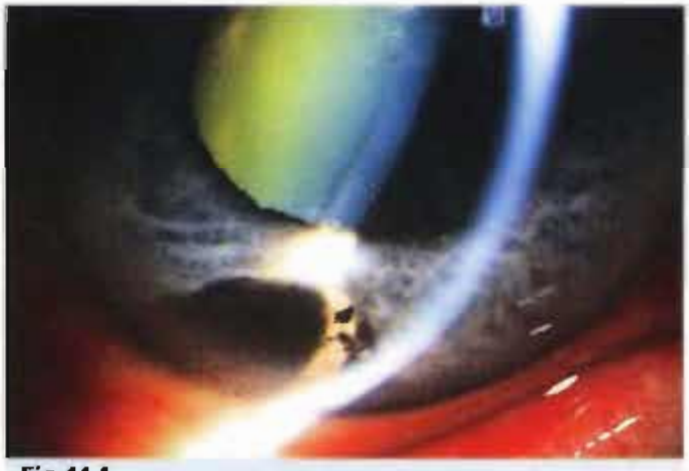

Fig. 11.1
Pigmented iris melanoma

Fig. 11.4
Tapioca iris melanoma (Courtesy of B. Damato)

b. Rare variants

- Diffusely growing intrastromal melanoma may give rise to ipsilateral hyperchromic heterochromia.
- 'Tapioca melanoma' is characterized by multiple surface nodules (Fig. 11.4).

Treatment

1. **Observation** of suspicious lesions involves documentation by slit-lamp examination, gonioscopy and photography. Follow-up should be lifelong because growth may occur after several years of apparent inactivity. Initially the patient is reviewed after 3–6 months, then 6–9 months and later annually.
2. **Iridectomy** for small tumours with iris reconstruction to reduce postoperative photophobia.
3. **Iridocyclectomy** for tumours invading the angle (Fig. 11.5).
4. **Radiotherapy** with local plaques (brachytherapy) or external irradiation with charged particles for non-resectable tumours.
5. **Enucleation** may be required for diffusely growing tumours.

Differential diagnosis

1. **Iris naevus**, if large and distorting the pupil (*see* Fig. 11.11).
2. **Ciliary body melanoma** with extension through the iris root (*see* Fig. 11.24).
3. **Metastasis** to the iris is rare and usually occurs in patients with a known systemic malignancy. It is a pink or yellow, fast-growing mass (Fig. 11.6) which may be associated with anterior uveitis and occasionally hyphaema. Small, multiple deposits may also be seen (Fig. 11.7).
4. **Adenoma of the iris pigment epithelium** is a rare benign tumour characterized by a dark grey-black nodule with a smooth but sometimes multinodular surface, most frequently in the peripheral iris (Fig. 11.8). The lesion causes anterior displacement and thinning of the iris stroma, which eventually erodes, disclosing the tumour on slit-lamp biomicroscopy.
5. **Leiomyoma** is an extremely rare benign tumour which arises from smooth muscle. The appearance is similar to that of an amelanotic melanoma except that it is not necessarily confined to the inferior half of the iris (Fig. 11.9). Often the diagnosis can be established only histologically.
6. **Primary iris cyst** (*see* below).

Fig. 11.5
Gonioscopic view of iris melanoma involving the angle

Fig. 11.7
Multiple iris metastases (Courtesy of B. Damato)

Fig. 11.6
Solitary iris metastasis

Fig. 11.8
Adenoma of the iris pigment epithelium

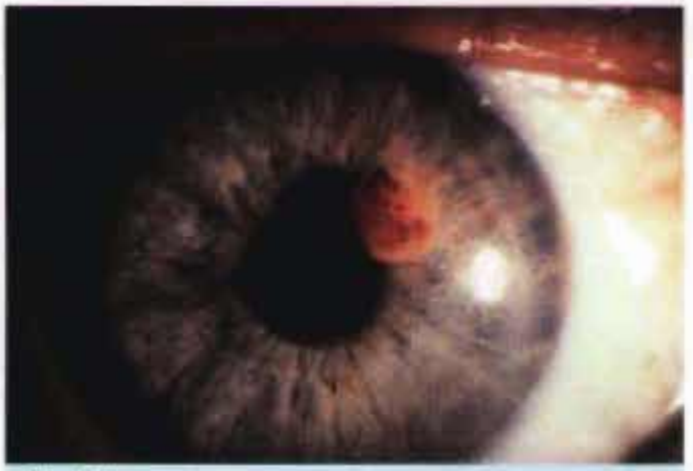

Fig. 11.9
Iris leiomyoma

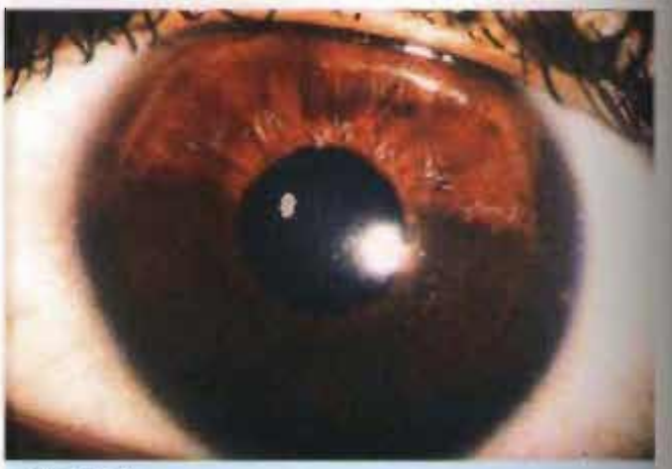

Fig. 11.12
Diffuse iris naevus

Fig. 11.10
Iris naevus and freckles

Fig. 11.13
Lisch nodules

Fig. 11.11
Iris naevus distorting the pupil

Iris naevi

1. **A typical naevus** is a pigmented, flat or slightly elevated lesion, usually less than 3mm in diameter (Fig. 11.10). It is located in the superficial layers and may occasionally cause mild distortion of the pupil and ectropion uveae (Fig. 11.11).
2. **A diffuse naevus** obscures normal iris crypts and gives rise to hyperchromic heterochromia (Fig. 11.12). It may be seen in patients with the *Cogan–Reese syndrome* (see Chapter 9) and may also show small pedunculated nodules resembling mammillations.
3. **Lisch nodules** are multiple, small, bilateral, melanocytic hamartomas found after the age of 16 years in virtually all patients with neurofibromatosis-1 (Fig. 11.13).
4. **Freckles** are smaller than naevi (see Fig. 11.10). They are frequently multiple and bilateral, but never distort the iris architecture.

Iris cysts

Primary cysts

Primary iris cysts are rare curiosities arising from the pigment epithelium or, rarely, the stroma. The vast majority,

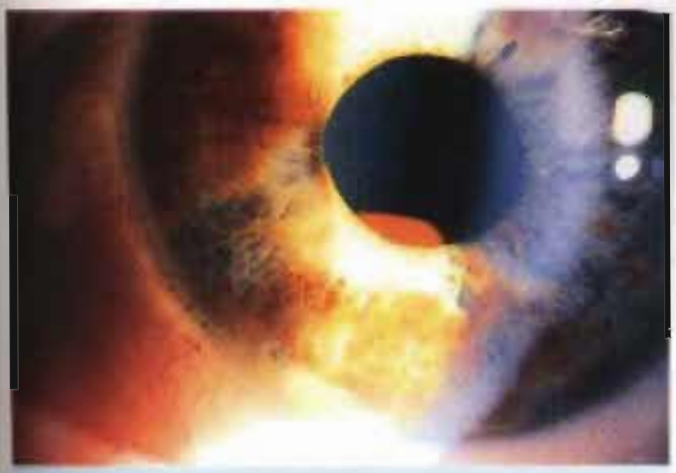

Fig. 11.14
Pupillary epithelial iris cyst

Fig. 11.16
Primary stromal iris cyst

Fig. 11.15
Mid-zonal epithelial iris cyst

Fig. 11.17
Primary stromal iris cyst containing a fluid–debris level

particularly those arising from the pigment epithelium, are stationary and asymptomatic.

1. **Epithelial** cysts are unilateral, solitary, dark-brown, globular structures which transilluminate. They may be located at the pupillary border (Fig. 11.14), in the mid-zone (Fig. 11.15) or the iris root. Occasionally the cysts become dislodged and float freely in the anterior chamber or vitreous. The vast majority are innocuous and rarely require treatment.
2. **Stromal** cysts present in the first year of life. They are solitary, unilateral, have a smooth, translucent anterior wall and contain fluid (Fig. 11.16). The cyst may remain dormant for many years or suddenly enlarge and cause secondary glaucoma, corneal decompensation and show a fluid–debris level reminiscent of a pseudo-hypopyon (Fig. 11.17). Occasionally the cyst may break free from the iris and float in the anterior chamber or migrate to another location. Although spontaneous regression can occur, most require treatment by needle aspiration or surgical excision.

Fig. 11.18
Secondary iris cyst containing a worm

Secondary cysts

Secondary iris cysts develop as a result of implantation, parasites (Fig. 11.18), tumours or the prolonged use of

Fig. 11.19
Secondary iris cysts due to topical administration of long-acting miotics

Fig. 11.20
Secondary iris cyst following corneal grafting

Fig. 11.21
Sentinel vessels associated with ciliary body melanoma
(Courtesy of B. Damato)

long-acting miotics. The latter are usually bilateral, small, multiple and located along the pupillary border (Fig. 11.19). Their development can be prevented by the use of topical 2.5% phenylephrine. Implantation cysts originate by deposition of surface epithelial cells from the conjunctiva or cornea on the iris after penetrating or surgical trauma and may lead to the following:

1. **Pearl** cysts are small, white, solid lesions with opaque walls located in the stroma and are not connected to the wound.
2. **Serous** cysts are translucent, filled with fluid and may be connected to the wound (Fig. 11.20). They frequently enlarge, leading to corneal oedema, anterior uveitis and glaucoma. Ultrasound biomicroscopy may show the location and extent of the lesions when surgical excision is contemplated.

Ciliary body tumours

Ciliary body melanoma

About 10% of uveal melanomas arise from the ciliary body.

Clinical features

1. **Presentation** is in the sixth decade with visual symptoms but occasionally the tumour may be discovered incidentally
2. **Signs** depend on the size and location of the tumour. Small localized tumours cannot usually be visualized without pupillary dilatation and gonioscopy.
   - Dilated episcleral blood vessels in the same quadrant as the tumour (sentinel vessels) (Fig. 11.21).
   - Extraocular extension through the scleral emissary vessels may produce a dark epibulbar mass (Fig. 11.22) which may be mistaken for a conjunctival melanoma.
   - Pressure on the lens may give rise to astigmatism, subluxation or cataract (Fig. 11.23).
   - Erosion through the iris root may mimic iris melanoma (Fig. 11.24).
   - Retinal detachment may be caused by posterior extension.

Fig. 11.22
Extraocular extension of ciliary body melanoma

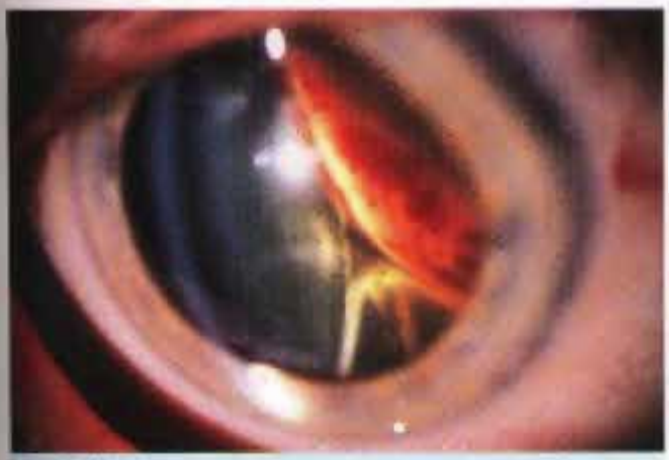

Fig. 11.23
Ciliary body melanoma displacing the lens (Courtesy of C. Barry)

Fig. 11.24
Ciliary body melanoma eroding the iris root

- Anterior uveitis, caused by tumour necrosis, is uncommon.
- Circumferential (annular) growth for 360° carries the worst prognosis because early diagnosis is difficult.

Investigations

1. **Triple-mirror contact lens** examination through a well-dilated pupil is essential and is particularly useful in detecting forward erosion through the iris root into the angle.
2. **Transillumination** may give an approximate indication of tumour extent but is of little diagnostic value because an amelanotic melanoma may transilluminate.
3. **Ultrasonic biomicroscopy** is useful in eyes with opaque media and also shows dimensions and extent.
4. **Biopsy** may be helpful in selected cases.

Treatment

1. **General considerations** (*see* choroidal melanoma below).
2. **Enucleation** for large tumours and those affecting the anterior choroid. Secondary glaucoma, resulting from extensive invasion of Schlemm canal, is also an indication for enucleation.
3. **Iridocyclectomy** for small or medium-sized tumours involving no more than one-third of the angle. Complications are vitreous haemorrhage, retinal detachment and incomplete resection.
4. **Radiotherapy** by brachytherapy or external beam irradiation in selected cases.

Differential diagnosis

1. **Uveal effusion syndrome** (*see* Fig. 12.66) may resemble circumferential ciliary body melanoma. However, the effusion is lobulated, transilluminates brightly and appears cystic on ultrasonography.
2. **Congenital epithelial iridociliary cysts** may displace the lens but can be readily differentiated from melanomas by ultrasonography.
3. **Other ciliary body tumours**, which are extremely rare, include medulloepithelioma, metastases, adenocarcinoma, cystic adenoma and leiomyoma. In most of these the correct diagnosis can be made only histologically.

Choroidal tumours

Choroidal melanoma

Melanoma of the choroid is the most common primary intraocular tumour in adults and accounts for 85% of uveal melanomas.

Clinical features

1. **Presentation** is usually during the sixth decade (range fifth to eighth) in one of the following ways:

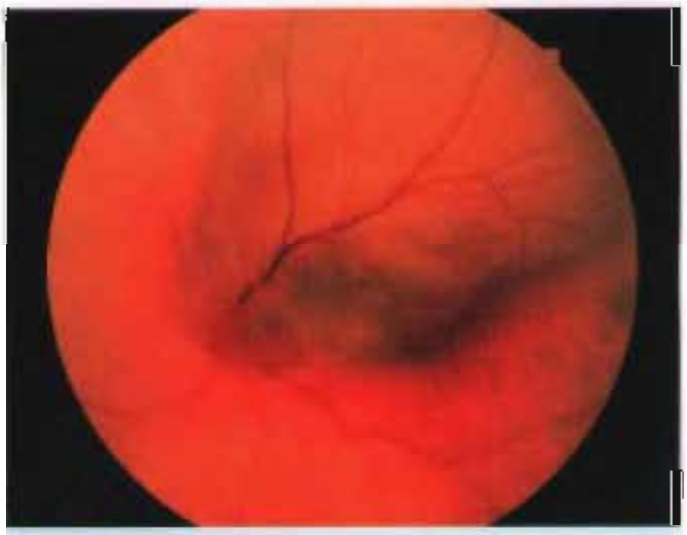

Fig. 11.25
Choroidal melanoma

- An asymptomatic tumour detected by chance.
- A symptomatic tumour causing decreased visual acuity or a visual field defect.
- About a third of patients complain of very brief 'balls of light' travelling across the visual field two to three times a day, most apparent in subdued lighting.

2. **Signs**
   - An elevated, subretinal, dome-shaped, brown or grey mass (Fig. 11.25). Occasionally the tumour may be mottled with dark-brown or black pigment, or be virtually amelanotic (Fig. 11.26). Surface orange pigment (lipofuscin) is common but not diagnostic.
   - If the tumour breaks through Bruch membrane it acquires a mushroom-shaped appearance (Fig. 11.27).

Fig. 11.26
Amelanotic choroidal melanoma

Fig. 11.27
Mushroom-shaped choroidal melanoma with surface lipofuscin (Courtesy of D. Lehman)

Fig. 11.28
B-scan ultrasonogram showing a choroidal melanoma and secondary retinal detachment

   - A secondary exudative detachment is common and must not be mistaken for a rhegmatogenous detachment.
   - Occasional features include choroidal folds, haemorrhage, secondary glaucoma, cataract and uveitis.

Investigations

1. **Binocular indirect ophthalmoscopy** is sufficient for accurate diagnosis in the vast majority of cases.
2. **Indirect slit-lamp biomicroscopy** detects subtle features associated with relatively small tumours, such as the presence of lipofuscin pigment, subretinal fluid, cystoid changes in the overlying sensory retina and dilated vessels within the tumour.
3. **Ultrasonography** is used to determine tumour size and detect extraocular extension. B-scan ultrasonography shows the anterior border of the tumour as well as acoustic hollowness, choroidal excavation and orbital shadowing (Fig. 11.28).
4. **FA** is of limited diagnostic value because there is no pathognomonic pattern. Most melanomas show a 'dual circulation' (Fig. 11.29b and c), mottled fluorescence during the arteriovenous phase and progressive leakage and staining (Fig. 11.29d).
5. **ICG** is superior to FA because there is less interference caused by RPE changes, better visualization of the tumour and choroidal vessels, and superior definition of tumour margins.
6. **MRI**, particularly when combined with surface coils and fat suppression sequences, shows that choroidal melanomas are hyperintense in T1-weighted (Fig. 11.30) and hypointense in T2-weighted images, but these features are not pathognomonic.
7. **Colour-coded Doppler** imaging may differentiate pigmented tumours from intraocular haemorrhage, particularly in eyes with opaque media.
8. **Fine-needle aspiration biopsy** is used occasionally to obtain cellular aspirates for analysis where the diagnosis cannot be established by less invasive methods.

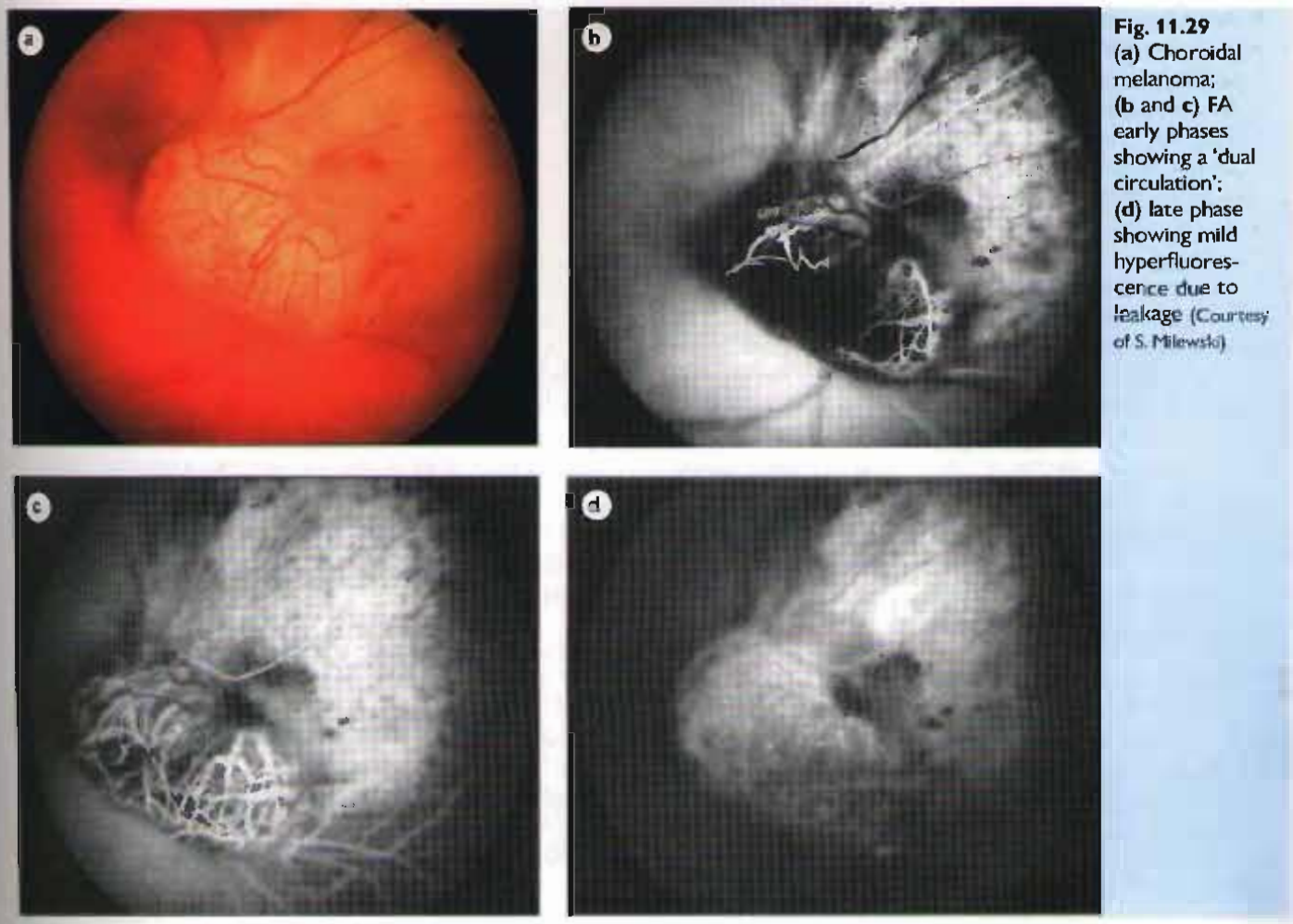

Fig. 11.29
(a) Choroidal melanoma; (b and c) FA early phases showing a 'dual circulation'; (d) late phase showing mild hyperfluorescence due to leakage (Courtesy of S. Milewski)

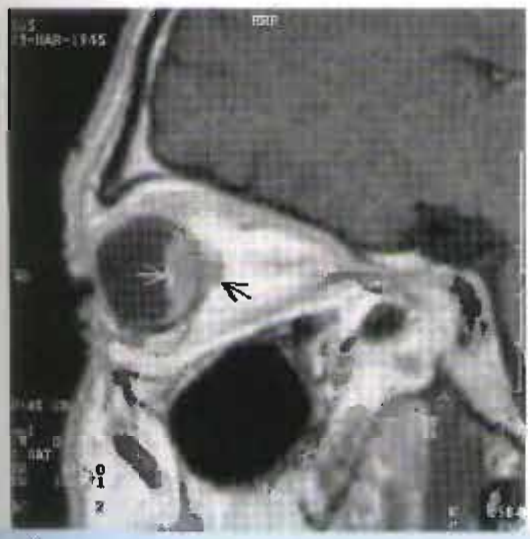

Fig. 11.30
T1-weighted MRI scan showing a choroidal melanoma (white arrow) and extraocular extension (black arrow) (Courtesy of M Karolczak-Kulesza)

9. **General medical examination** is aimed at:
   - Excluding a metastasis to the choroid, which occurs most frequently from the bronchus in both sexes and the breast in women. Occasionally, the primary site is the kidney or gastrointestinal tract. Initial investigations should include chest radiography, rectal examination and mammography in females.
   - Detecting metastatic spread *from* the choroid as this would influence management. For example, a patient with overt metastatic disease would not be subjected to enucleation of a painless eye. The liver is by far the most frequent site for metastases. Hepatic involvement can be detected by ultrasonography and elevated gamma-glutamyl transpeptidase and alkaline phosphatase levels. Chest radiography should also be performed to detect possible lung secondaries but these are rare without liver metastases.

Treatment

This is complex and should be tailored to the individual patient. The following factors are considered: (a) size, location, extent and apparent activity of the tumour, (b) state of the fellow eye, (c) general health and age of the patient and (d) the patient's wishes and fears. For instance, treatment may be inappropriate for a slowly growing tumour in the only eye of a very elderly or chronically ill patient. There is an increasing trend towards the use of combined therapy with the following modalities:

1. **Brachytherapy** is frequently the treatment of first choice because it is relatively straightforward and effective.
   a. ***Indications*** are tumours less than 10 mm in elevation and less than 20 mm in basal diameter in which there is a reasonable chance of salvaging vision. Supplemental transpupillary thermotherapy may be required to enhance the results. Tumour regression starts about 1–2 months after treatment and continues for several years.
   b. ***Complications*** include retinopathy, papillopathy, vitreous haemorrhage, cataract and recurrence of tumour.
   c. ***Cure rate*** is similar to that following enucleation of comparable tumours.
2. **External radiotherapy** with protons or helium ions by means of a cyclotron unit. The advantages over brachytherapy are that the beam can be more highly focused, affording a more homogeneous dose of radiation. Treatment is fractionated over 4 days, with each dose delivered over a 30-second period.
   a. ***Indications*** are tumours unsuitable for brachytherapy either because of size or posterior location to within 4 mm of the disc or fovea.
   b. ***Complications***, which are more common following treatment of large tumours, include loss of lashes, eyelid depigmentation, canaliculitis with epiphora, conjunctival keratinization, keratitis, exudative retinal detachment and neovascular glaucoma.
   c. ***Cure rate*** is similar to that following brachytherapy or enucleation.
3. **Transpupillary thermotherapy** (TTT) is performed with a diode laser to induce hyperthermia but not coagulation.
   a. ***Indications*** are selected small tumours, particularly if pigmented and located near the fovea or optic disc. TTT is also a complementary modality to brachytherapy.
   b. ***Complications*** include visual field defects and maculopathy.
4. **Trans-scleral local resection** is a difficult procedure which involves excision of the tumour with a rim of healthy choroid under a partial-thickness scleral flap. The procedure is performed under systemic arterial hypotension.
   a. ***Indications*** are carefully selected tumours that are too thick for radiotherapy and usually less than 16mm in diameter.
   b. ***Complications*** include haemorrhage, retinal detachment, cataract and tumour recurrence.
5. **Stereotactic radiosurgery** with the Gamma-knife is a new method involving single-session delivery of ionizing radiation to a stereotactically localized volume of tissue. This modality is an alternative to charged particle irradiation or enucleation in treating large tumours with preservation of visual function in selected cases.
6. **Enucleation**
   a. ***Indications*** for excision of the globe are very large tumours, particularly if all useful vision has been irreversibly lost. In these cases, enucleation is preferred to brachytherapy because the dose of radiation required to reach the apex of the tumour would be too great to salvage the rest of the globe.
   b. ***Technique*** should be meticulous to avoid dissemination of malignant cells. The procedure should be performed with gentle isolation and section of the extraocular muscles, and minimal traction on the optic nerve when cutting. About 4 weeks after enucleation, the patient can be fitted with an artificial eye.
7. **Exenteration** of the orbit is indicated for patients with extensive extraocular extension at the time of diagnosis or for orbital recurrences following enucleation.
8. **Palliation** with chemotherapy and/or immunotherapy may prolong life in patients with metastatic disease. In patients with lung metastases, life expectancy is generally <1 year and, when the liver is involved, <6 months.

Modified Callender classification of uveal melanomas

1. **Spindle cell melanomas**, which make up 45% of all tumours, are composed of spindle cells, with a small proportion described as fascicular because of the palisading or ribbon-like arrangement of cells in parallel rows (Fig. 11.31).
2. **Pure epithelioid cell melanomas** make up 5% (Fig. 11.32).
3. **Mixed cell melanomas**, containing spindle and epithelioid cells, account for 45% (Fig. 11.33).
4. **Necrotic melanomas**, in which the predominant cell type is unrecognizable, make up the remaining 5% (Fig. 11.34).

Prognostic factors

1. **Histological features** implying an adverse prognosis include large numbers of epithelioid cells per high-power field, closed vascular loops within the tumour and lymphocytic infiltration.

Fig. 11.31
Fascicular spindle cell melanoma (Courtesy of A Garner)

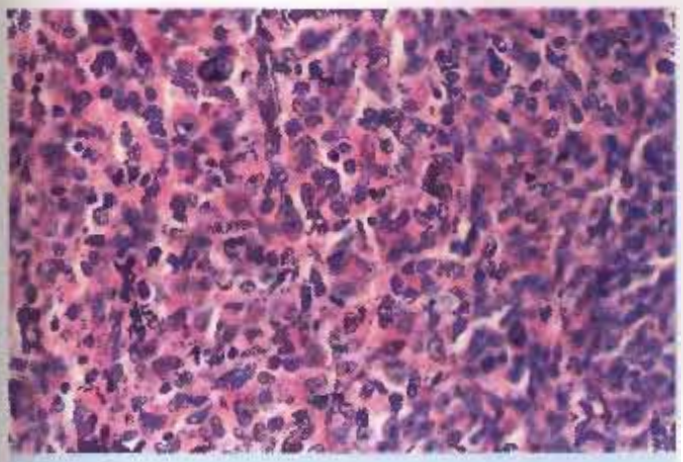

Fig. 11.32
Epithelioid cell melanoma (Courtesy of A. Garner)

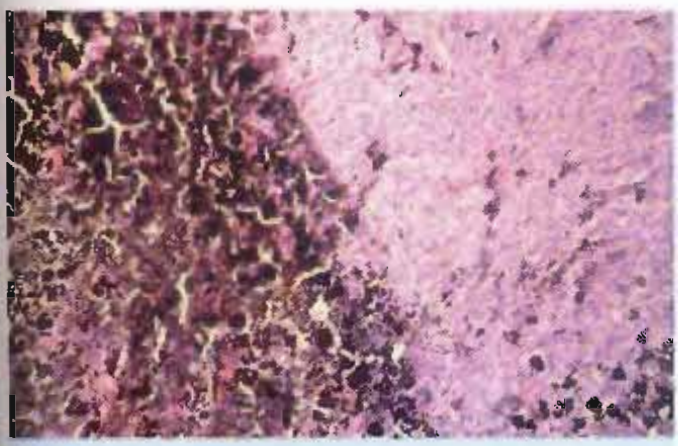

Fig. 11.33
Mixed cell melanoma (Courtesy of A. Garner)

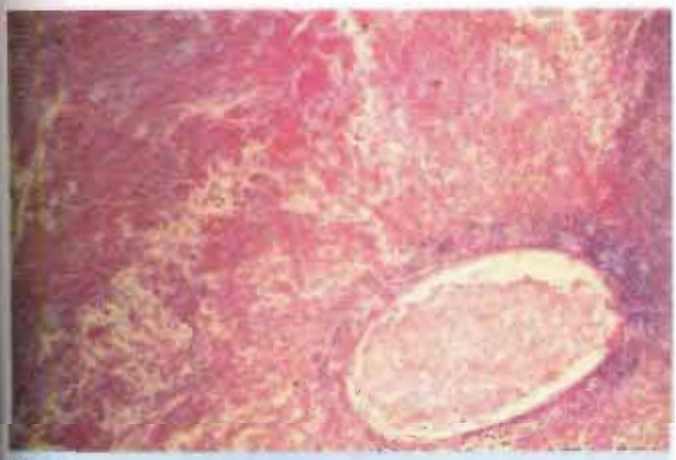

Fig. 11.34
Necrotic melanoma (Courtesy of A. Garner)

2. **Chromosomal abnormalities** within the melanoma cells are associated with a very poor prognosis, with a 50% death rate at 5 years.
3. **Large tumours** have a worse prognosis than small tumours. Following enucleation, 5-year mortality is as follows:
   - Small tumours (<10 mm in diameter): 16%.
   - Medium tumours (10–15 mm in diameter): 32%.
   - Large tumours: 53%.
4. **Extrascleral extension** carries a very poor prognosis.
5. **Location**: anterior tumours have a worse prognosis because they are usually diagnosed later than those near the posterior pole.
6. **Patients over the age of 65 years** have a worse prognosis than younger patients.

Differential diagnosis

Although in the vast majority of cases the diagnosis is straightforward, the following conditions should be considered in the differential diagnosis of atypical cases, particularly amelanotic melanomas:

1. **Other choroidal tumours**, most notably large naevi, circumscribed haemangiomas and solitary metastases.
2. **Solitary choroidal granulomas** associated with sarcoidosis or tuberculosis.
3. **Posterior scleritis** (*see* Chapter 7).

Choroidal naevus

Choroidal naevi are present in about 5% of the general population but are less common in fair-skinned individuals. Although they are probably present at birth, growth occurs mainly during the pre-pubertal years and is extremely rare thereafter. For this reason the rare event of clinically detectable growth should arouse suspicion of malignant transformation.

Signs

1. **Typical naevus**
   - An asymptomatic, oval or circular, slate-blue or green-grey lesion with detectable but not sharp borders which may be associated with surface drusen (Fig. 11.35 and *see* Fig. 11.38a).
   - Dimensions are <5 mm in diameter and 1 mm or less in thickness.
2. **A suspicious naevus** has one or more of the following characteristics:
   - Presence of symptoms, such as metamorphopsia or photopsia.
   - Dimensions >5 mm in diameter and >1 mm in thickness (Fig. 11.36).
   - Clumps of surface orange (lipofuscin) pigment (Fig. 11.37).
   - Absence of surface drusen on a thick lesion.
   - Location of the posterior margin of the lesion within 3 mm of the optic disc.
   - Serous retinal detachment either over the surface of the lesion or inferiorly.

NB: The greater the number of these features, the higher the chance that the lesion is a melanoma.

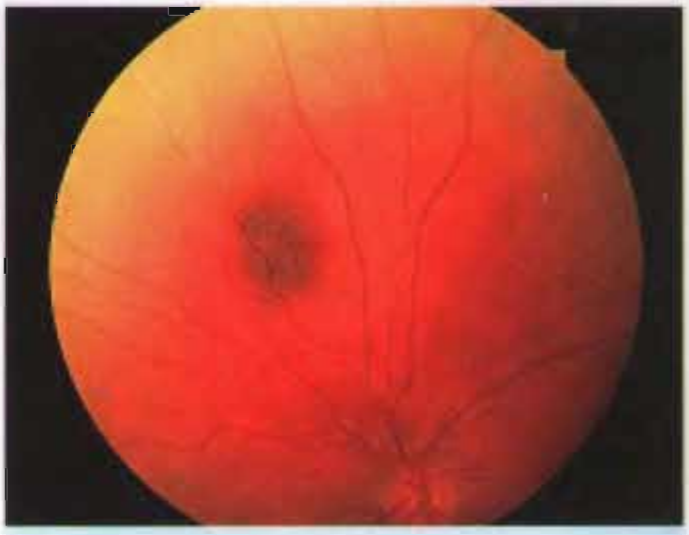

Fig. 11.35
Typical choroidal naevus

Fig. 11.36
Suspicious choroidal naevus

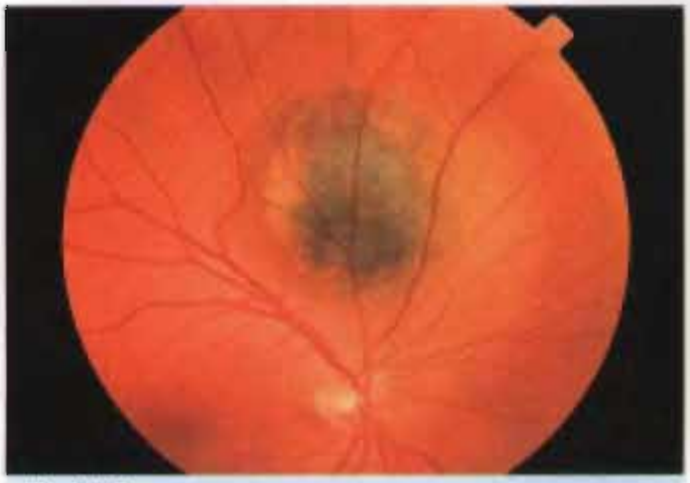

Fig. 11.37
Suspicious choroidal naevus with surface lipofuscin

Investigations

1. **FA** findings depend on the amount of pigmentation within the naevus and associated changes in the overlying RPE. Most choroidal naevi are avascular and pigmented, giving rise to hypofluorescence caused by blockage of background choroidal fluorescence. If the naevus is associated with surface drusen, this will result in areas of hyperfluorescence (Fig. 11.38b). FA is, however, not helpful in distinguishing a small melanoma from a naevus.
2. **Ultrasonography** shows a localized flat or slightly elevated lesion with high internal reflectivity (Fig. 11.39).

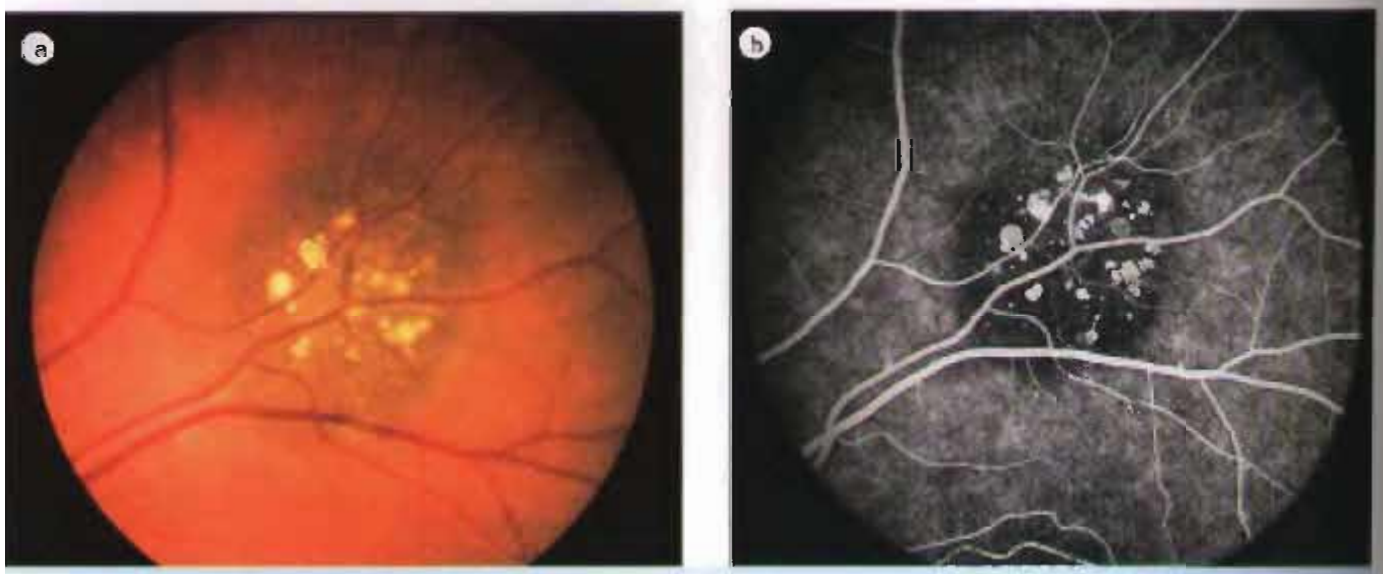

Fig. 11.38
(a) Typical choroidal naevus with surface drusen; (b) FA showing blockage of background fluorescence and hyperfluorescence of surface drusen

Fig. 11.39
B-scan ultrasonogram of choroidal naevus (see *text*) (Courtesy of M Karolczak-Kulesza)

Fig. 11.40
Circumscribed choroidal haemangioma (Courtesy of J.A. Shields and A. Singh)

Management

1. **Typical naevi** do not require follow-up because the risk of malignant transformation is extremely low.
2. **Suspicious naevi** should be evaluated initially every 3–6 months and then 9–12 months with fundus photography and ultrasonography to detect the possibility of growth. Although it is difficult to detect small changes in thickness by ultrasonography, careful comparison of fundus photographs, with special attention to the location of landmarks such as blood vessels, is usually a reliable method of documenting growth. Once growth has been documented, the lesion should be reclassified as a choroidal melanoma and managed accordingly.

Circumscribed choroidal haemangioma

Circumscribed choroidal haemangioma is a rare, benign, vascular hamartoma which is probably present at birth but does not become symptomatic until years later. The tumour is almost always solitary and is not associated with systemic disease. Most are stationary and a few are slow-growing.

Clinical features

1. **Presentation** is in the fourth to fifth decades with unilateral central visual impairment.
2. **Signs**
   - A dome-shaped or placoid, orange-red, mass which blends with the surrounding choroid (Fig. 11.40). Subtle white foci may be present on the surface of the tumour and probably represent fibrous metaplasia of the overlying RPE.
   - The lesion usually measures 3–9 mm in diameter and is most commonly located in the juxtapapillary or macular area.
3. **Complications** include secondary cystoid retinal degeneration overlying the tumour, exudative retinal detachment, macular invasion, RPE degeneration and subretinal fibrosis.

Special investigations

1. **Ultrasonography** shows an oval or placoid lesion with a sharp anterior border and high internal reflectivity, but no choroidal excavation or orbital shadowing (Fig. 11.41).
2. **FA** reveals filling during the choroidal phase (Fig. 11.42a), progressive hyperfluorescence during the venous phase and late leakage (Fig. 11.42b).

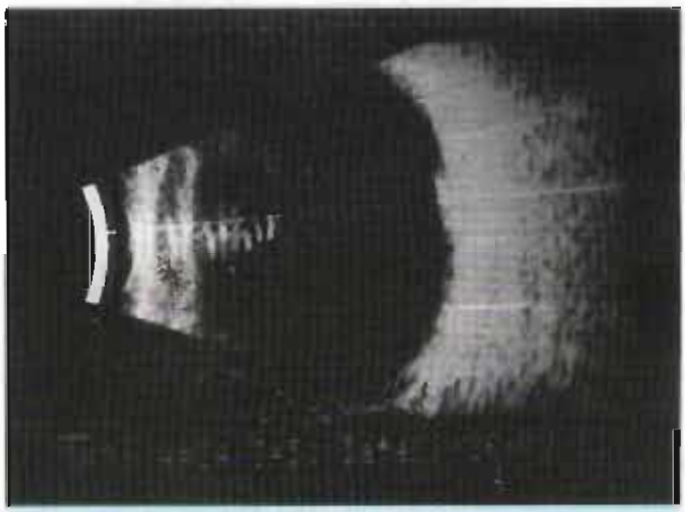

Fig. 11.41
B-scan ultrasonogram of circumscribed choroidal haemangioma (see *text*) (Courtesy of S. Milewski)

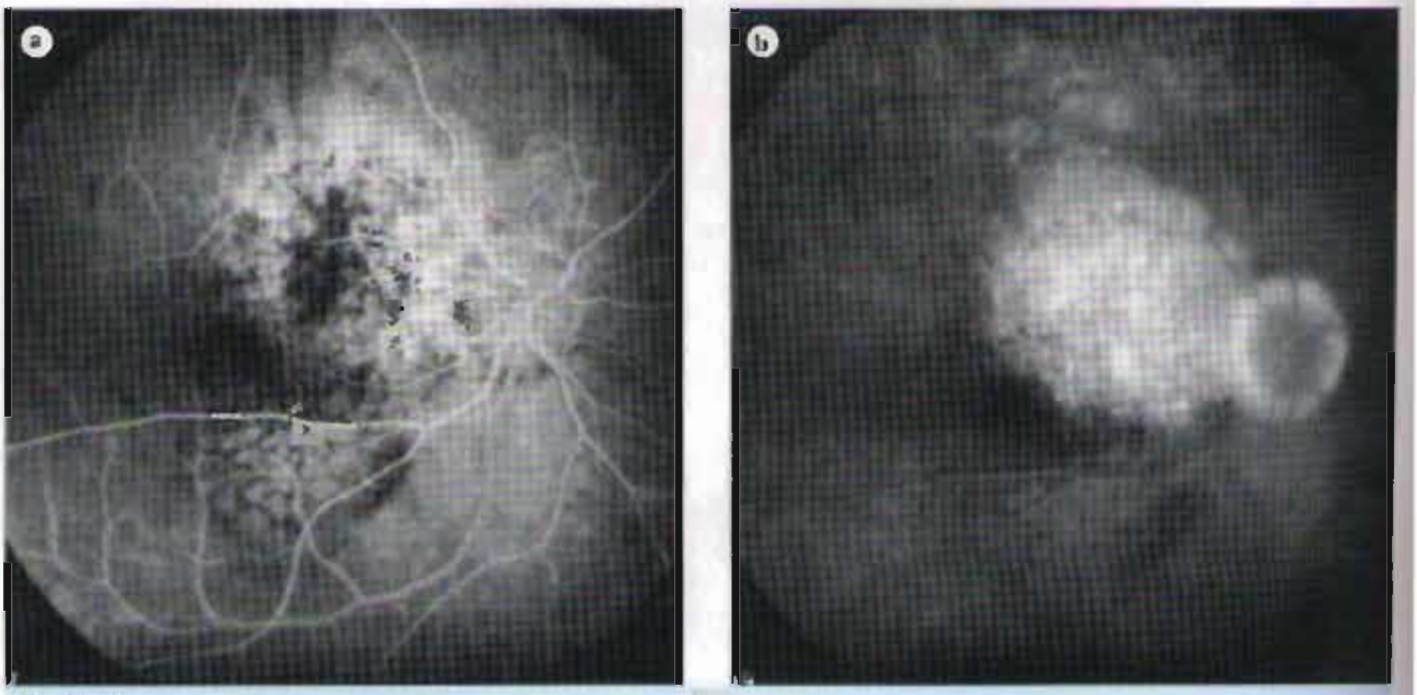

Fig. 11.42
FA of circumscribed choroidal haemangioma. (a) Early phase showing hyperfluorescence due to filling; (b) late phase showing leakage (Courtesy of S. Milewski)

Treatment

Vision-threatening lesions may be treated as follows:

1. **Transpupillary thermotherapy** for lesions not involving the macula. Indocyanine green can be administered as an adjunct to enhance uptake of diode laser energy.
2. **Radiotherapy** either by low-dose lens-sparing external beam irradiation or brachytherapy.

Diffuse choroidal haemangioma

The diffuse choroidal haemangioma usually affects over half of the choroid and enlarges very slowly. It occurs in patients with the Sturge–Weber syndrome ipsilateral to the naevus flammeus (*see* Chapter 20).

1. **Presentation** is in the third decade with visual impairment.
2. **Signs.** Thickening of the choroid and a deep-red 'tomato ketchup' colour which is most marked at the posterior pole (Fig. 11.43).
3. **Complications** include secondary retinal cystoid degeneration and exudative retinal detachment.
4. **Treatment** is by external beam radiotherapy.

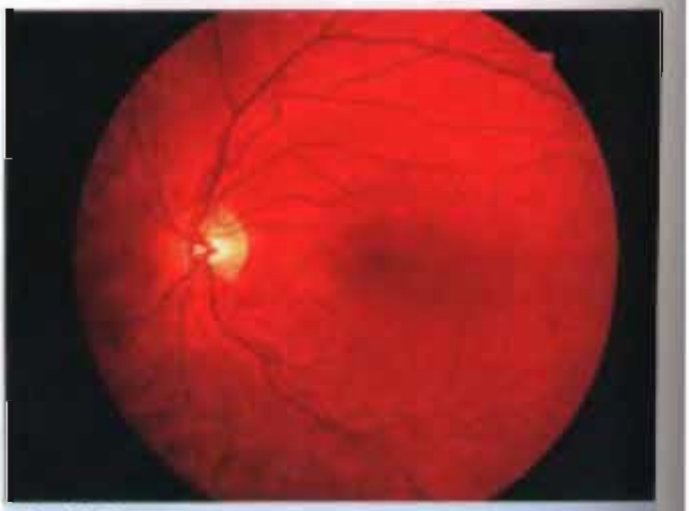

Fig. 11.43
Diffuse choroidal haemangioma

Metastatic tumours

The choroid is by far the most common site for uveal metastases, accounting for about 90%, followed by the iris and ciliary body. Metastatic tumours to the choroid are more common than primary malignancies but their presence is usually undetected or overshadowed by the patient's general illness. The most frequent primary site is the breast in women and the bronchus in both sexes. A choroidal secondary may be the initial presentation of a bronchial carcinoma, whereas a past history of breast cancer is the rule in patients with breast secondaries. Other less common primary sites include the gastrointestinal tract, kidney and skin melanoma. The prostate is, however, an extremely rare primary site. Patient survival is generally poor, with a median of 8–12 months for all patients and 15–17 months for those with breast carcinoma. In patients with breast carcinoma risk factors for choroidal metastases include dissemination of disease in more than one organ and the presence of lung and brain metastases.

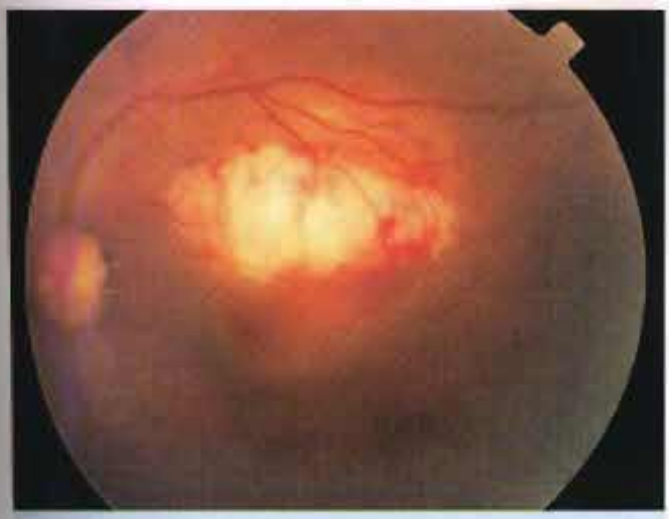

Fig. 11.44
Choroidal metastasis from colon carcinoma (Courtesy of S. Milewski)

Fig. 11.46
Ultrasonogram of choroidal metastasis (*see text*) (Courtesy of M. Karolczak-Kulesza)

Clinical features

1. **Presentation** is usually with visual impairment although metastases may be asymptomatic if located away from the macula.
2. **Signs**
   - A fast-growing, creamy-white, placoid or oval lesion most frequently located at the posterior pole (Fig. 11.44).
   - The tumour seldom becomes significantly elevated because it infiltrates laterally (Fig. 11.45).
   - Occasionally the deposits assume a globular shape and may mimic an amelanotic melanoma.
   - The deposits may be multiple and both eyes are involved in 10–30% of cases.
   - Secondary exudative retinal detachment is frequent and may occur in eyes with relatively small deposits.

Special investigations

1. **Ultrasonography** shows diffuse choroidal thickening and moderate internal acoustic reflectivity (Fig. 11.46).
2. **FA** shows early hyperfluorescence (Fig. 11.47b) with diffuse late staining (Fig. 11.47c and d) but in contrast with choroidal melanomas a 'dual circulation' does not occur.

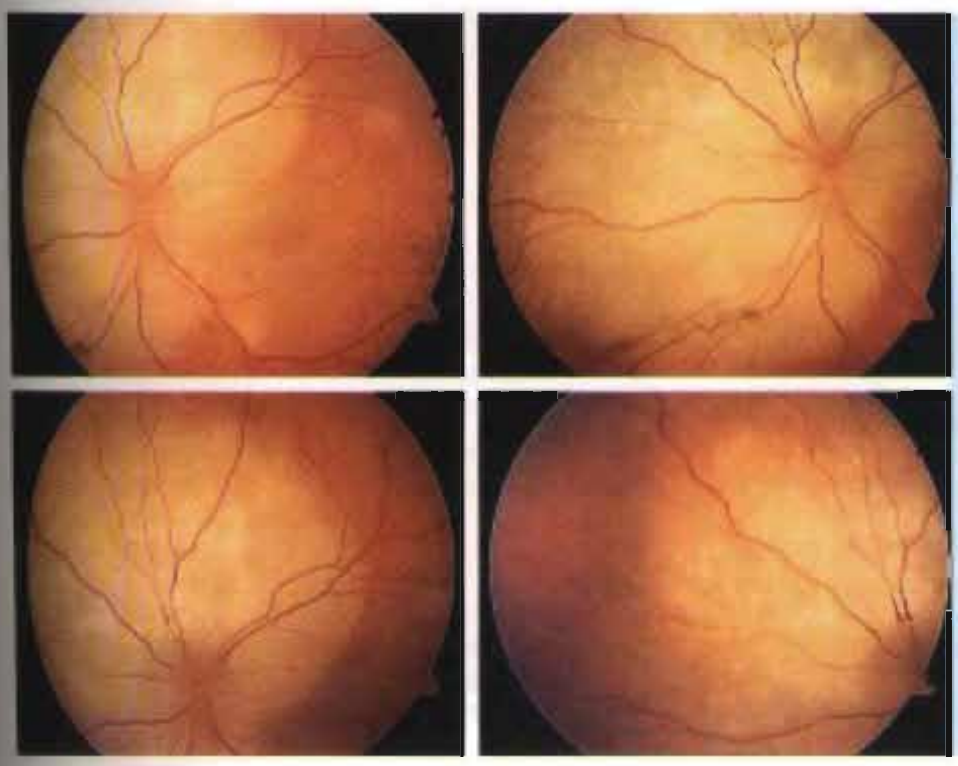

Fig. 11.45
Choroidal metastasis from breast carcinoma (Courtesy of M. Karolczak-Kulesza

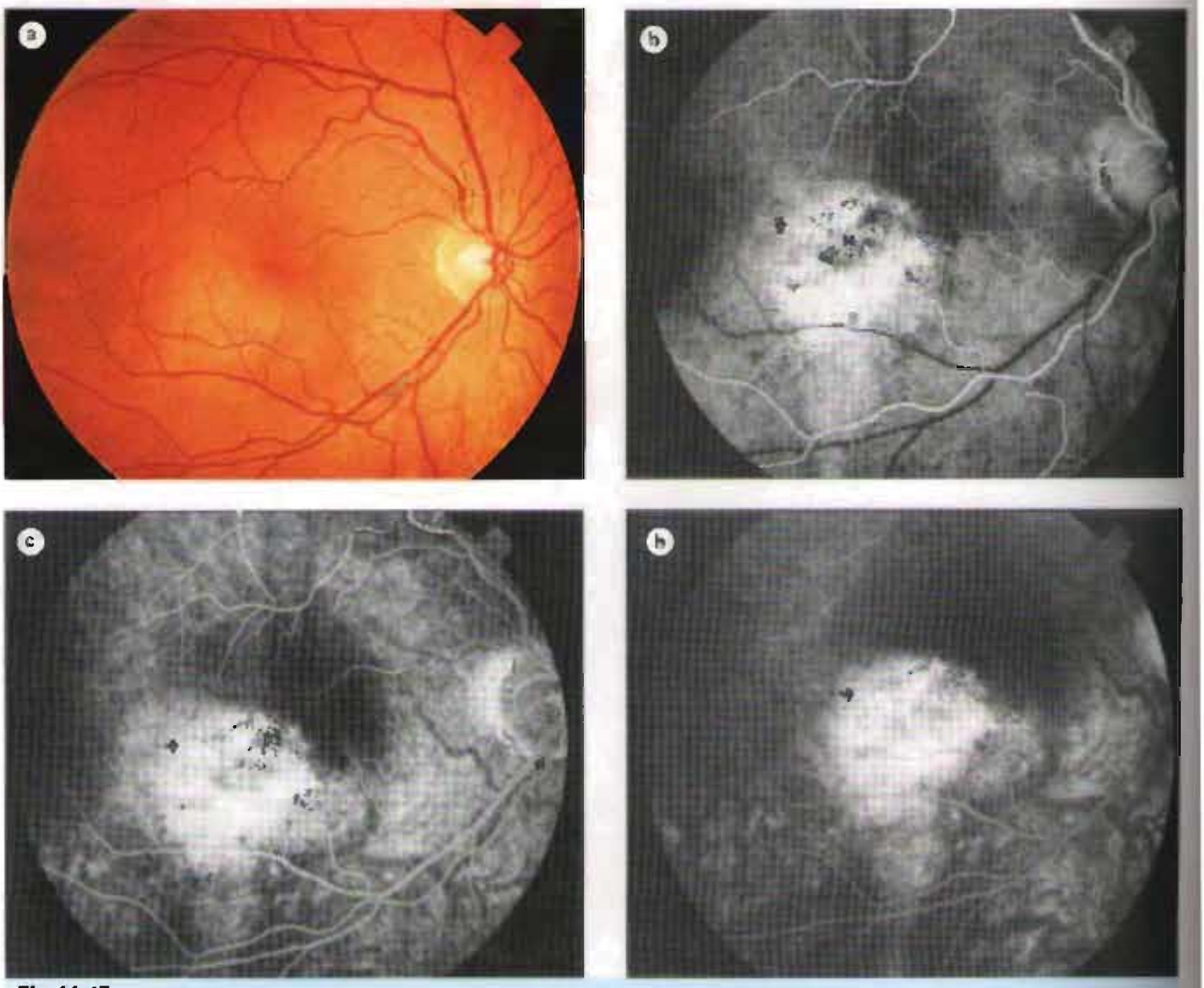

Fig. 11.47
(a) Choroidal metastasis; (b) FA arterial phase showing hyperfluorescence but absence of a 'dual circulation'; (c, d) late phases showing staining (Courtesy of S. Milewski)

3. **Biopsy**, performed either trans-sclerally or by fine-needle aspiration, may be useful.
4. **Systemic** investigations to detect the primary tumour, if unknown, or other metastatic sites.

Treatment

1. **Observation**, if the patient is asymptomatic or receiving systemic chemotherapy.
2. **Radiotherapy**, either external beam or brachytherapy, for small tumours.
3. **Transpupillary thermotherapy** is useful for deposits of moderate thickness and minimal amount of subretinal fluid.
4. **Systemic therapy** for the primary tumour may be beneficial for choroidal metastases.
5. **Enucleation** may be required for a painful blind eye.

Choroidal osseous choristoma

Choroidal osseous choristoma (osteoma) is a very rare, benign, very slow-growing, ossifying tumour which typically affects healthy young women. Both eyes are affected in about 25% of cases but not usually simultaneously.

1. **Presentation** is in the second to third decades with gradual visual impairment if the macular is involved.
2. **Signs.** An orange-yellow lesion with well-defined scalloped borders, most commonly situated at the posterior pole (Fig. 11.48). The tumour grows very slowly with the development of overlying RPE changes (Fig. 11.49).
3. **Complications.** Secondary choroidal neovascularization is common and responds poorly to laser photocoagulation.
4. **FA** shows a diffuse mottled pattern of hyperfluorescence during the early and late phases.

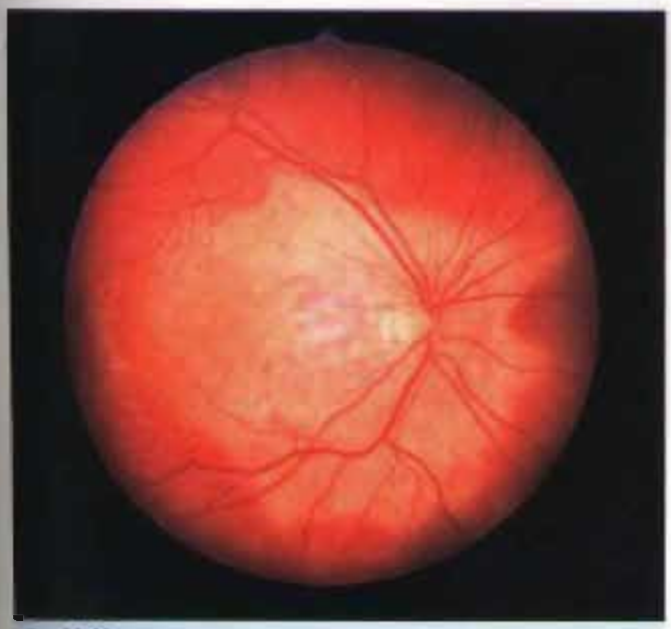

Fig. 11.48
Choroidal osseous choristoma

Fig. 11.49
Same eye several years later showing overlying RPE changes

5. **Ultrasonography** shows a very dense highly reflective lesion (bone) which renders silent the orbital tissue behind it (Fig. 11.50).

Melanocytoma

Melanocytoma is a benign, heavily pigmented tumour that may occur anywhere in the uveal tract, but arises most frequently from dendritic uveal melanocytes in the lamina cribrosa of the optic nerve head. Anterior uveal melanocytomas may undergo acute necrosis with resultant uveitis, pigment dispersion and secondary glaucoma. In contrast with choroidal melanoma, melanocytoma typically affects dark-skinned individuals, although it may also occur in white people.

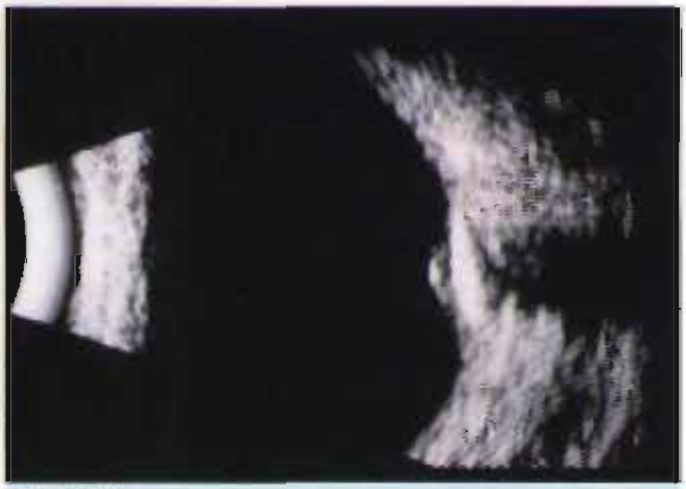

Fig. 11.50
Ultrasonogram of choroidal osseous choristoma (see *text*)

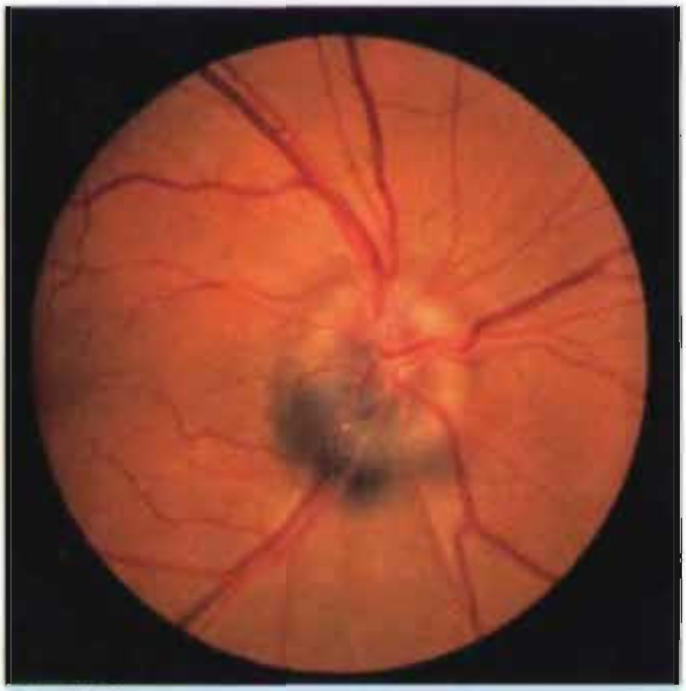

Fig. 11.51
Melanocytoma of the optic nerve head

1. **Presentation** of optic nerve head melanocytoma is usually by chance, although a deep-seated tumour may cause optic nerve dysfunction.
2. **Signs**. A black lesion with feathery edges frequently occupying the inferior part of the disc (Fig. 11.51). Occasionally, the tumour is elevated and occupies the entire disc surface.
3. **Complications**, which are rare, include malignant transformation and central retinal vascular obstruction secondary to spontaneous tumour necrosis.
4. **Treatment** is not required except in the very rare event of malignant transformation.
5. **Differential diagnosis** includes choroidal melanoma invading the optic nerve head and reactive RPE hyperplasia.

Lymphoma

Primary intraocular–central nervous system lymphoma is an uncommon, diffuse, highly malignant, large B-cell (non-Hodgkin) lymphoma. It arises within the brain, spinal cord, leptomeninges and/or the eye and has a poor prognosis, with a 5-year survival rate of less than 33%.

CNS features

1. **At presentation** the following four profiles are seen:
   - Solitary or multiple intracranial nodules.
   - Diffuse meningeal or periventricular lesions.
   - Localized intradural spinal masses.
   - Intraocular involvement.
2. **The diagnosis** is usually made by identifying malignant lymphocytes in the brain, cerebrospinal fluid or vitreous.

Ocular features

Lymphoma tends to involve the vitreous and retina and frequently represents a diagnostic challenge, masquerading as uveitis. Ocular findings usually precede CNS involvement by months or a few years and only 20% of patients have ocular lesions at the time of diagnosis of CNS disease. Both eyes are eventually affected in 80% of cases, but the severity of involvement is often asymmetrical.

1. **Chronic anterior uveitis** unresponsive to steroids.
2. **Intermediate uveitis** in an elderly patient may initially be responsive to steroids but subsequently becomes unresponsive. The vitreous typically shows large clumps or sheets composed of malignant cells.
3. **Posterior segment**
   - Multifocal, large, yellowish, sub-RPE infiltrates are most commonly seen (Fig. 11.52). Coalescence of the lesions may form a ring which is pathognomonic for intraocular lymphoma (Fig. 11.53).
   - Less frequent manifestations include diffuse retinal infiltrates resembling viral retinitis, vascular sheathing and occlusion, and multifocal, tiny deep white lesions which can be misdiagnosed as inflammatory.
4. **Investigations** include neurological evaluation, MRI, lumbar puncture and vitreous biopsy.

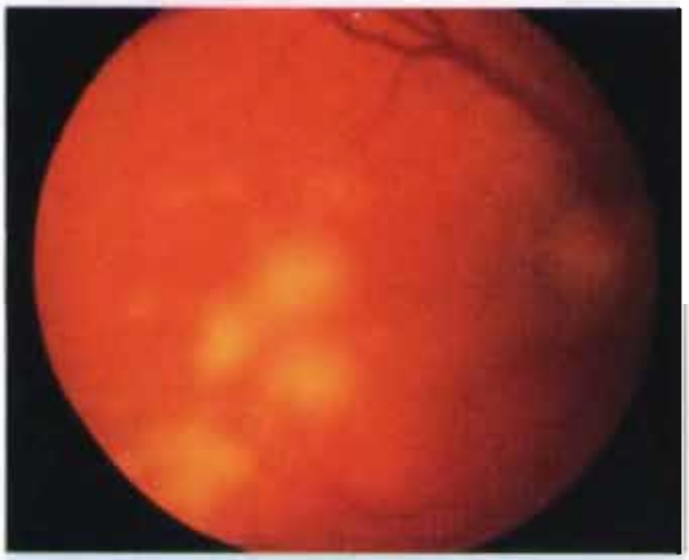

Fig. 11.52
Multifocal lymphomatous subretinal infiltrates (Courtesy of A. Cruess)

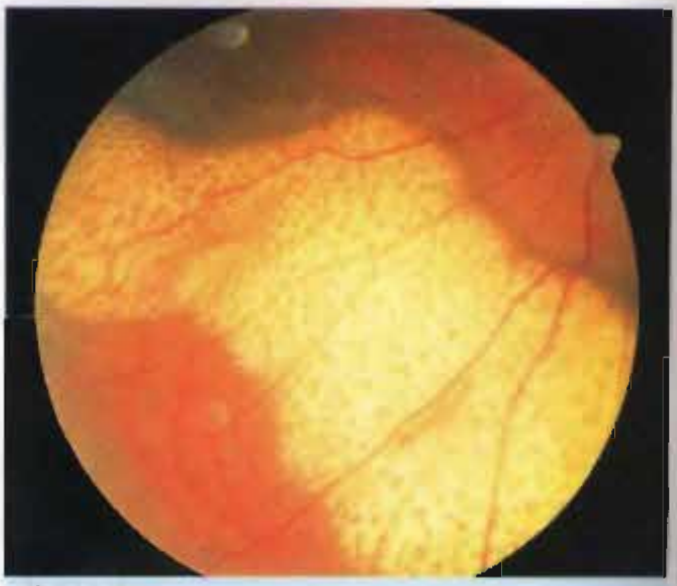

Fig. 11.53
Annular lymphomatous subretinal infiltration (Courtesy of B. Damato)

Treatment

1. **Systemic** treatment is with high-dose external beam radiotherapy to the eyes, sometimes in conjunction with whole brain radiotherapy, and/or systemic or intrathecal chemotherapy.
2. **Intravitreal** methotrexate may be used as primary treatment and for recurrences following systemic therapy.

Retinal and optic nerve head tumours

Retinoblastoma

Retinoblastoma is the most common primary intraocular malignancy of childhood. Even so, it is rare, occurring in about 1:20,000 live births and accounts for about 3% of all childhood cancers.

Genetics

Retinoblastoma results from malignant transformation of primitive retinal cells before final differentiation. Because these cells disappear within the first few years of life, the tumour is seldom seen after 3 years of age. Retinoblastoma

may be heritable or non-heritable. The predisposing gene (*RPE1*) is at 13q14.

1. **Heritable** (germline) retinoblastoma accounts for 40%. In these patients one allele of the *RPE1* (a tumour supressor gene) has mutated in all body cells. When a further mutogenic event ('second hit') affects the second allele, the cell undergoes malignant transformation. Because all the retinal precursor cells contain the initial mutation, these children develop bilateral and multifocal tumours. Familial cases also carry a predisposition to non-ocular cancers; most notably pincaloblastoma (trilateral retinoblastoma) and osteosarcoma. The risk of second malignancy increases greatly if external beam irradiation has been used to treat the original tumour, and the second tumour tends to arise within the irradiated field.
   - The risk of transmitting the gene mutation is 50%, and because of high penetrance 40% of offspring of a survivor of heritable retinoblastoma will develop the tumour.
   - Unaffected parents of a child with bilateral retinoblastoma with no family history have a 40% chance of producing another affected child.
   - Some familial cases present with initially unilateral disease and about 15% of patients with heritable retinoblastoma only express unilateral involvement.
2. **Non-heritable** (somatic) retinoblastoma accounts for 60% of cases. The tumour is unilateral, not transmissible and does not predispose the patient to an increased risk of second non-ocular cancers. Eighty-five per cent of patients with unilateral retinoblastoma fall into this category.

Presentation

The vast majority present within the first 2 years of life. Children with bilateral tumours tend to present earlier (average 12 months) than those with unilateral involvement.

1. **Leukocoria** (white pupillary reflex) is the commonest (60%) (Fig. 11.54).
2. **Strabismus** is the second most common (20%). Fundus examination is therefore mandatory in all cases of childhood strabismus.

Fig. 11.54
Left leukocoria due to advanced retinoblastoma (Courtesy of C. Bary)

Fig. 11.55
Multiple iris nodules due to invasion by retinoblastoma

Fig. 11.56
Pseudo-hypopyon due to anterior segment invasion by retinoblastoma

3. **Secondary glaucoma**, sometimes associated with buphthalmos, is uncommon.
4. **Unilateral iris invasion** in older children (average age 6 years) may manifest as multifocal nodules (Fig. 11.55), resembling granulomatous inflammation, or pseudohypopyon (masquerade syndrome) (Fig. 11.56). It is therefore important to consider retinoblastoma in the differential diagnosis of unusual chronic uveitis in children.
5. **Orbital inflammation** mimicking orbital or preseptal cellulitis may occur with necrotic tumours (Fig. 11.57). It does not necessarily imply extraocular extension and the exact mechanism is not known.
6. **Orbital invasion** may occur in neglected cases (Fig. 11.58).
7. **Metastatic disease** involving regional lymph nodes and brain before the detection of ocular involvement is rare.
8. **Raised intracranial pressure** due to 'trilateral retinoblastoma' before the diagnosis of ocular involvement is very rare.
9. **On routine examination** of a patient known to be at risk.

Fig. 11.57
Orbital inflammation associated with retinoblastoma

Fig. 11.58
Orbital invasion by neglected retinoblastoma

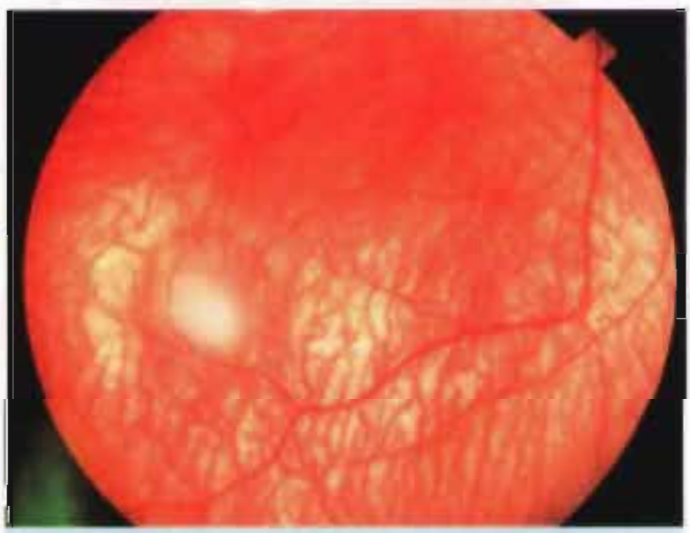

Fig. 11.59
Small intraretinal retinoblastoma

Fig. 11.60
Retinoblastoma

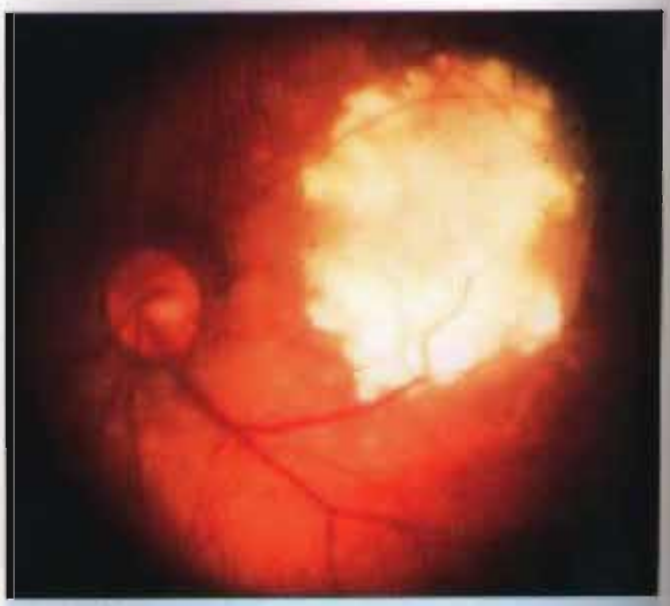

Fig. 11.61
Endophytic retinoblastoma (Courtesy of C. Barry)

Signs

Indirect ophthalmoscopy with scleral indentation must be performed on *both eyes* after full mydriasis. This is because without indentation pre-equatorial tumours may be missed and one eye may harbour multiple tumours. The clinical signs depend on tumour size and growth pattern.

1. **An early intraretinal** tumour is a placoid white lesion (Figs 11.59 and 11.60).
2. **An endophytic** tumour grows inwards towards the vitreous, projecting from the retinal surface as a white, cottage cheese-like mass, with surface blood vessels (Fig. 11.61).
3. **An exophytic** tumour grows outwards as a subretinal, multilobulated white mass (Fig. 11.62). It detaches the retina and may be difficult to visualize if the subretinal fluid is deep (Fig. 11.63).

Fig. 11.62
Exophytic retinoblastoma (Courtesy of S. Milewski)

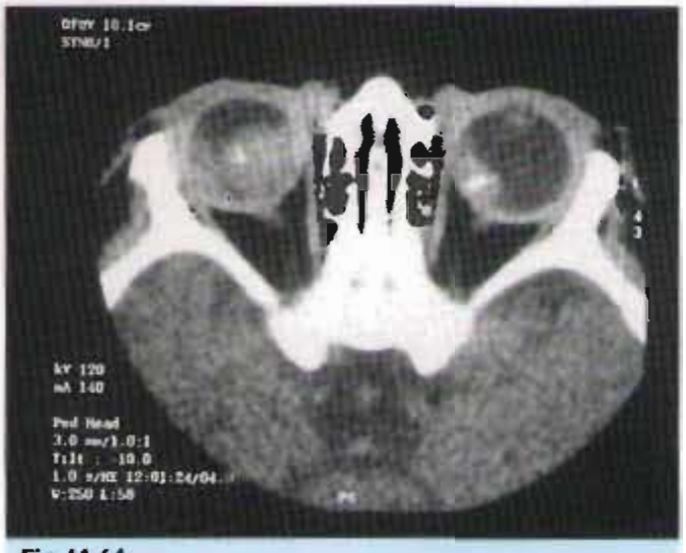

Fig. 11.64
CT scan showing bilateral advanced retinoblastomas (Courtesy of K. Nischal)

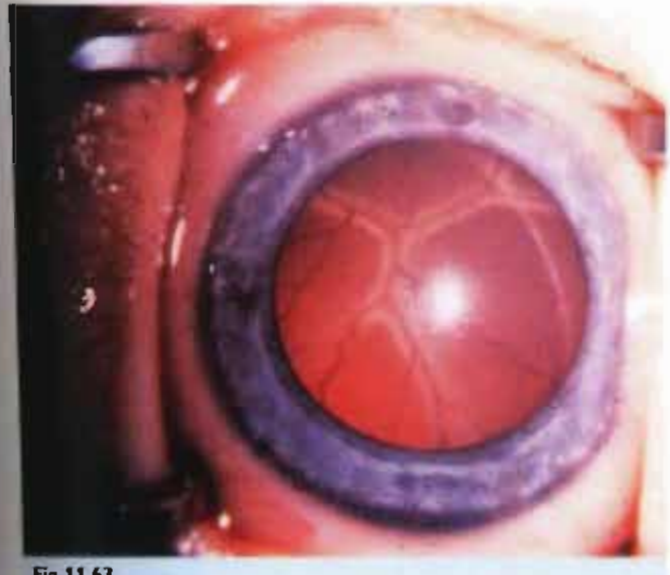

Fig. 11.63
Retinal detachment caused by exophytic retinoblastoma

Special investigations

1. **Ultrasonography** is used mainly to assess tumour size. It also detects calcification within the tumour and is helpful in the diagnosis of simulating lesions such as Coats disease and toxocariasis.
2. **CT** demonstrates gross involvement of the optic nerve, orbital and CNS extension, and the presence of pinealoblastoma and calcification (Fig. 11.64). However, it entails a significant dose of radiation which may be dangerous in patients with germinal mutations.
3. **MRI** cannot detect calcification, but is superior to CT for optic nerve evaluation and detection of a pinealoblastoma, especially when contrast is used. MRI may also be useful to differentiate retinoblastoma from simulating conditions.
4. **Systemic investigations** such as bone marrow aspiration and lumbar puncture are performed only in patients with optic nerve involvement or evidence of extraocular extension.

Treatment

Treatment is related to tumour size, location and associated findings such as retinal detachment, subretinal and vitreous tumour seeds and the state of the fellow eye.

1. **Small tumours**, no more than 4 mm diameter and 2 mm thickness without vitreous or subretinal seeds can be treated with transpupillary thermotherapy laser or cryo-

Fig. 11.65
Small peripheral retinoblastoma seen on scleral indentation

therapy. The latter is particularly useful for pre-equatorial tumours which are difficult to reach with laser (Fig. 11.65).

2. **Medium-size tumours**
   a. ***Brachytherapy*** is indicated for tumours of no more than 12 mm diameter and 6 mm thickness, which are unsuitable for thermotherapy or cryotherapy, provided there is no vitreous seeding. Following treatment the tumour regresses leaving a calcific residue (Fig. 11.66).
   b. ***Chemotherapy*** with carboplatin, vincristine and etoposide which may be combined with cyclosporin. The drugs are given intravenously in 3 week cycles over a 4–9 month period depending on disease severity. This may be followed by local treatment with cryotherapy or thermotherapy to consolidate tumour control.

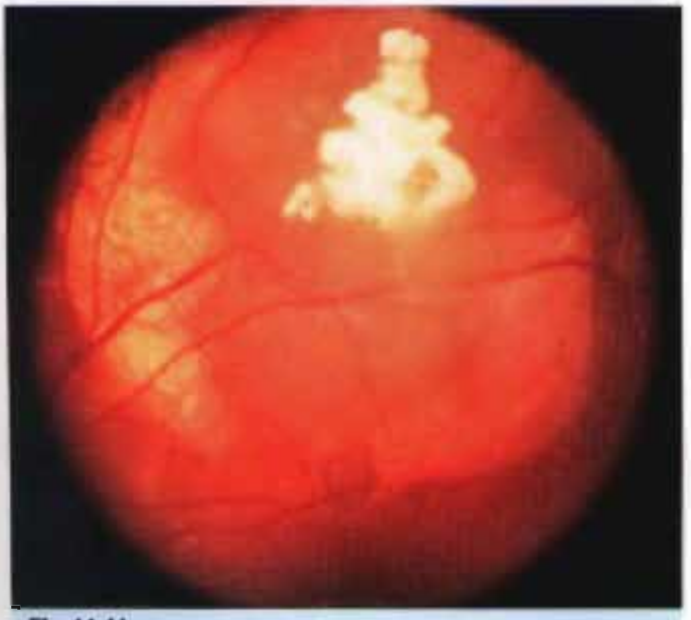

Fig. 11.66
Regressed retinoblastoma with calcific residue

Fig. 11.67
Large retinoblastoma with new surface vessels

   c. ***External beam radiotherapy*** should be avoided, if possible, due to the high risk of complications such as cataract formation, radiation retinopathy and cosmetic deformities. In patients with germinal mutations there is also a risk of inducing a second malignancy such as sarcoma of bone or connective tissue.
3. **Large tumours** (Fig. 11.67)
   a. ***Chemotherapy*** to shrink the tumour (chemoreduction), facilitating subsequent local treatment, thereby avoiding enucleation or external beam radiotherapy. Chemotherapy also will have a beneficial effect if a smaller tumour is present in the fellow eye.
   b. ***Enucleation*** if chemoreduction fails or a normal fellow eye makes aggressive chemotherapy inappropriate. It is also useful for diffuse retinoblastoma because of poor visual prognosis and high risk of recurrence with other therapeutic modalities. Enucleation should be performed with minimal manipulation and it is imperative to obtain a long piece of optic nerve (8–12 mm). There is no contraindication to the insertion of an orbital implant. Unfortunately subsequent shortening of the fornices and retraction of the implant (post-enucleation socket syndrome) may require further surgical intervention.
4. **Extraocular extension** beyond the lamina cribrosa is treated with chemotherapy after enucleation. Extension to the cut end of the optic nerve, or extension through the sclera, is treated with chemotherapy and irradiation of the affected orbit.
5. **Metastatic disease** is treated with high-dose chemotherapy. Patients with malignant cells in the cerebrospinal fluid may require intrathecal methotrexate.

Prognostic factors

The overall mortality rate is 2–5% and is related to the following:

1. **Tumour size and location.** Small posterior tumours do best but there is no significant difference between endophytic and exophytic types.

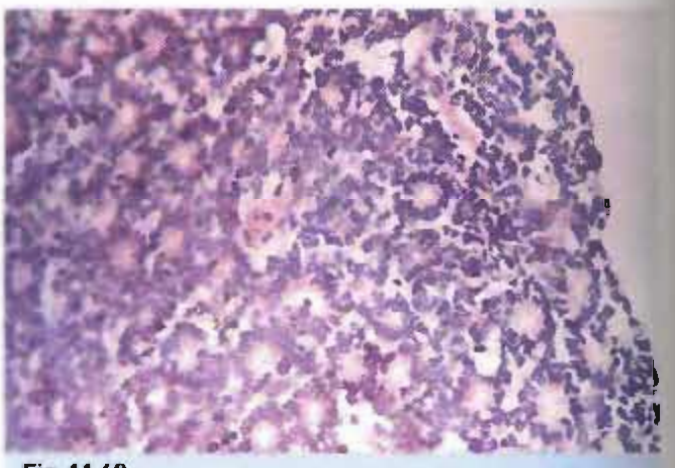

Fig. 11.68
Well-differentiated retinoblastoma with abundant rosettes
(Courtesy of A. Garner)

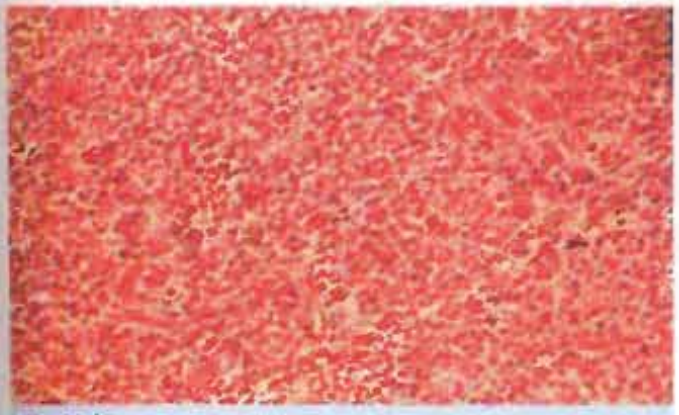

Fig. 11.69
Highly undifferentiated retinoblastoma (Courtesy of A. Garner)

Fig. 11.71
Persistent hyperplastic primary vitreous

Fig. 11.70
Leukocoria associated with persistent hyperplastic primary vitreous

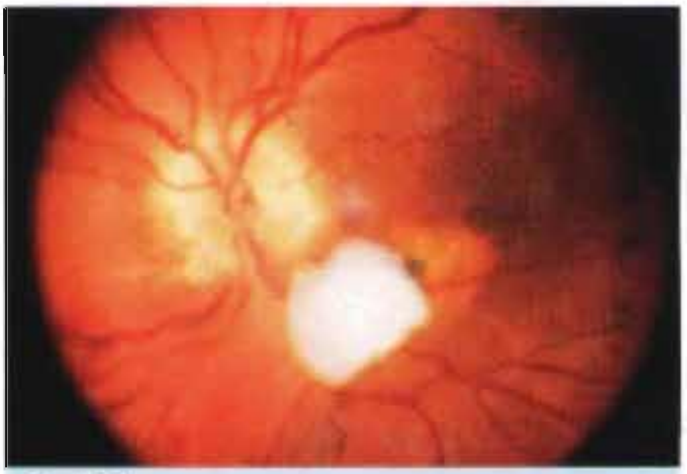

Fig. 11.72
Toxocara granuloma resembling endophytic retinoblastoma

2. **Cellular differentiation.** The mortality rate of patients whose tumours have abundant rosettes (Fig. 11.68) is much less than in those with highly undifferentiated tumours (Fig. 11.69).
3. **Optic nerve involvement** beyond the point of surgical transection is associated with high mortality.
4. **Invasion** of the choroid or vortex veins facilitates haematogenous spread and is therefore of adverse prognostic significance.
5. **Extrascleral spread** carries a grave prognosis.

Differential diagnosis

1. **Persistent hyperplastic primary vitreous** is an important cause of congenital leukocoria (Fig. 11.70). It typically occurs in a microphthalmic eye and is almost always unilateral. It is characterized by a retrolental mass into which elongated ciliary processes are inserted (Fig. 11.71). With time the mass contracts and pulls the ciliary processes centrally so that they become visible through the pupil. An associated dehiscence involving the posterior capsule may lead to subsequent cataract formation.
2. **Coats disease** is almost always unilateral, more common in boys and tends to present later than retinoblastoma. It is characterized by telangiectatic retinal blood vessels, extensive intra- and subretinal yellow exudation and exudative retinal detachment (*see* Chapter 14).
3. **Retinopathy of prematurity**, if advanced, may cause retinal detachment and leukocoria. Diagnosis is usually straightforward because of the history of prematurity and low birth weight (*see* Chapter 14).
4. **Toxocariasis** (*see* Chapter 10).
   a. ***Chronic toxocara endophthalmitis*** may cause a cyclitic membrane and a white pupil.
   b. ***Toxocara granuloma*** at the posterior pole may resemble an endophytic retinoblastoma (Fig. 11.72).
5. **Intermediate uveitis** may mimic the diffuse infiltrating type of retinoblastoma seen in older children (*see* Chapter 10).
6. **Retinal dysplasia** is characterized by a congenital pink or white retrolental membrane in a microphthalmic eye, with a shallow anterior chamber and elongated ciliary processes. Unilateral cases are usually not associated with systemic abnormalities. Patients with bilateral involvement may

Fig. 11.73
Vesiculobullous dermatitis in incontinentia pigmenti

Fig. 11.74
Cicatricial retinal detachment in incontinentia pigmenti

have Norrie disease or Warburg, Patau and Edward syndromes.

7. **Incontinentia pigmenti** (Bloch–Sulzberger syndrome) is a rare X-linked dominant disorder affecting girls. It is characterized by vesiculobullous dermatitis (Fig. 11.73) on the trunk and extremities. Malformations of teeth, hair, nails, bones and central nervous system may also be present. About one-third of children develop cicatricial retinal detachment which may cause leukocoria in the first year of life (Fig. 11.74).
8. **Retinocytoma** (retinoma) is thought to be a benign variant of retinoblastoma. It is characterized by calcified mass associated with RPE alteration and chorioretinal atrophy (Fig. 11.75). The appearance is remarkably similar to that of a retinoblastoma following irradiation (*see* Fig. 11.66).
9. **Retinal astrocytoma** (*see* below).

Retinal astrocytoma

Astrocytoma of the retina or optic nerve head is a rare, benign, non-vision-threatening tumour. It may occur in

Fig. 11.75
Retinocytoma (Courtesy of K. Nischal)

Fig. 11.76
Nodular retinal astrocytoma

Fig. 11.77
Flat retinal astrocytoma (Courtesy of C. Barry)

isolation but is most frequently seen in patients with tuberous sclerosis (*see* Chapter 20). About 50% of patients with tuberous sclerosis have fundus astrocytomas, which may be multiple and are bilateral in about 15% of cases.

Signs

- A semi-translucent nodule (Fig. 11.76) or a white, relatively flat, well-circumscribed plaque (Fig. 11.77).
- Later, the tumour becomes more solid and white and may, on cursory examination, resemble retinoblastoma (Fig. 11.78).
- Multiple areas of calcification within a long-standing tumour may give rise to a fossilized, mulberry-like appearance (Fig. 11.79).

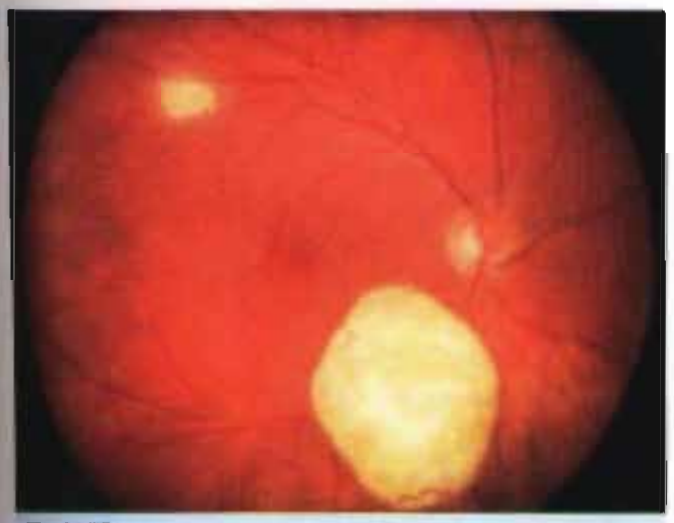

Fig. 11.78
Long-standing retinal astrocytomas

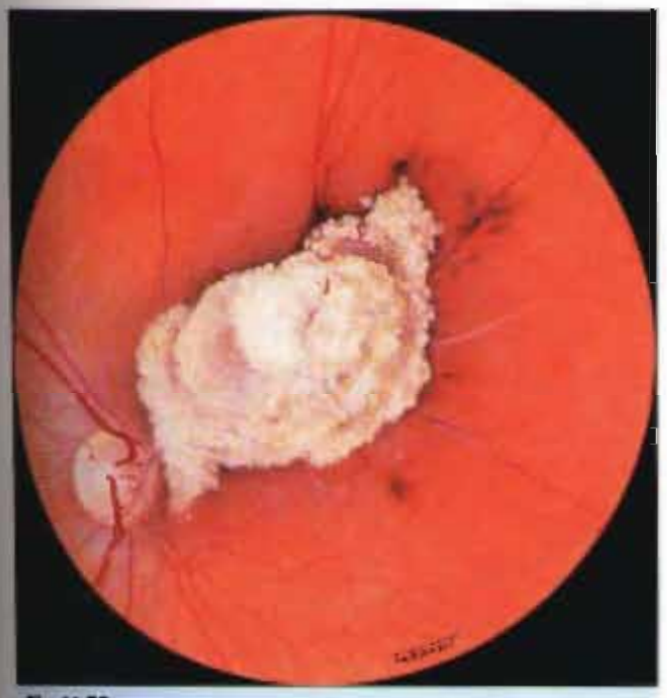

Fig. 11.79
Calcified mulberry-like retinal astrocytoma

Retinal capillary haemangioma

Capillary haemangioma of the retina or optic nerve head is a rare, sight-threatening vascular hamartoma which may occur in isolation (von Hippel disease). However about 50% of patients with solitary capillary haemangiomas and virtually all patients with multiple lesions have systemic disease. The combination of systemic and ocular lesions is referred to as the von Hippel–Lindau syndrome (V-H-L) (*see* Chapter 20). The prevalence of retinal capillary haemangiomas in patients with V-H-L is approximately 60%.

Endophytic

1. **Presentation** is in the second to third decades with unilateral or bilateral ocular involvement on screening, or with visual impairment.
2. **Signs** (in chronological order)
   - A tiny red lesion located within the capillary bed between an arteriole and a venule (Fig. 11.80).

Fig. 11.80
Early retinal capillary haemangioma

Fig. 11.81
Retinal capillary haemangioma (Courtesy of S. Milewski)

- A small, well-defined nodule (Fig. 11.81).
- A round orange-red mass associated with dilatation and tortuosity of the supplying artery and draining vein due to arteriovenous shunting so that both vessels appear similar (Fig. 11.82).

3. **FA** shows early hyperfluorescence (Fig. 11.83a) and late leakage (Fig. 11.83b).
4. **Complications** include hard exudate formation in the area surrounding the tumour and/or at the macula (*see* Fig. 11.85), macular oedema, epiretinal membrane formation, retinal detachment which may be tractional or exudative, and vitreous haemorrhage

Other types

1. **Exophytic haemangioma** is less common, arises from the outer retina in the juxtapapillary region and presents with visual loss. It is characterized by a sessile, ill-defined lesion with dilated blood vessels, which may be associated with retinal oedema and haemorrhage (Fig. 11.84). It carries a high risk of exudative retinal detachment.
2. **Optic nerve head haemangioma** (Fig. 11.85)

Fig. 11.84
Exophytic retinal capillary haemangioma (Courtesy of S. Milewski)

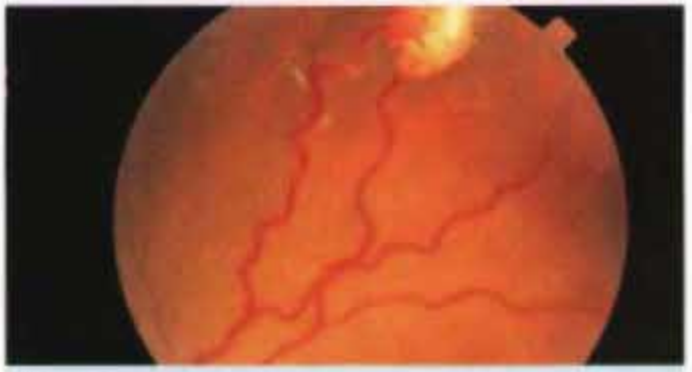

Fig. 11.82
Vascular dilatation and tortuosity associated with a retinal capillary haemangioma

Treatment

1. **Argon laser photocoagulation** for small peripheral lesions (Fig. 11.86a). Following successful treatment the calibre of the feeding blood vessels returns to normal (Fig. 11.86b).
2. **Cryotherapy** for larger peripheral lesions or those with exudative retinal detachment. Vigorous treatment of a large lesion may cause a temporary but extensive exudative retinal detachment.
3. **Brachytherapy** for lesions one to two disc diameters in size.
4. **Vitreoretinal surgery** may be required for non-absorbing vitreous haemorrhage, epiretinal fibrosis or tractional retinal detachment. If appropriate, the tumour may be destroyed by endolaser photocoagulation.

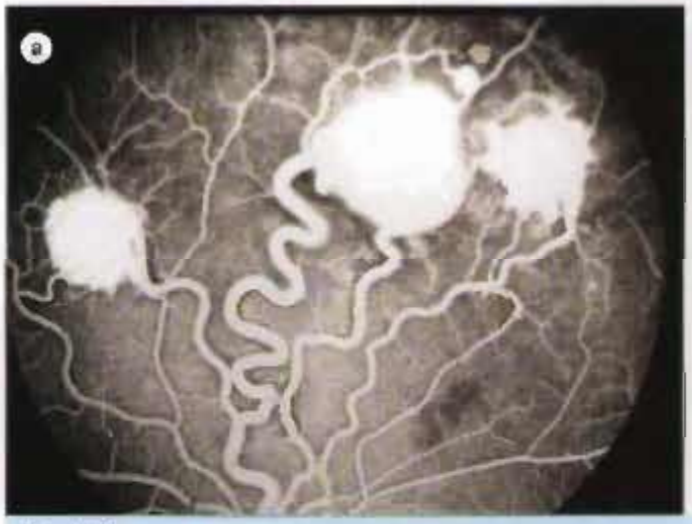

Fig. 11.83
(a) Early FA of multiple retinal capillary haemangiomas showing hyperfluorescence due to filling; (b) late phase showing leakage (Courtesy of S. Milewski)

Screening

Because it is impossible to predict which patients with retinal angiomas will also harbour systemic lesions, the ophthalmologist must refer all such patients for systemic and neurological evaluation. Relatives should also be screened because of the dominant inheritance pattern of the disease. Apart from physical examination, the following screening protocol should be regularly performed in patients with established V-H-L and relatives at risk:

1. **Annual screening**
   - Eye examination, physical examination and blood pressure measurement.
   - Renal ultrasonography from age 16 years.
   - Twenty-four hour urine collection for estimation of vanillyl mandelic acid and catecholamine levels from age 10 years to detect phaeochromocytoma.
2. **Screening every 3 years** involves abdominal and brain MRI scans from age 15 years.

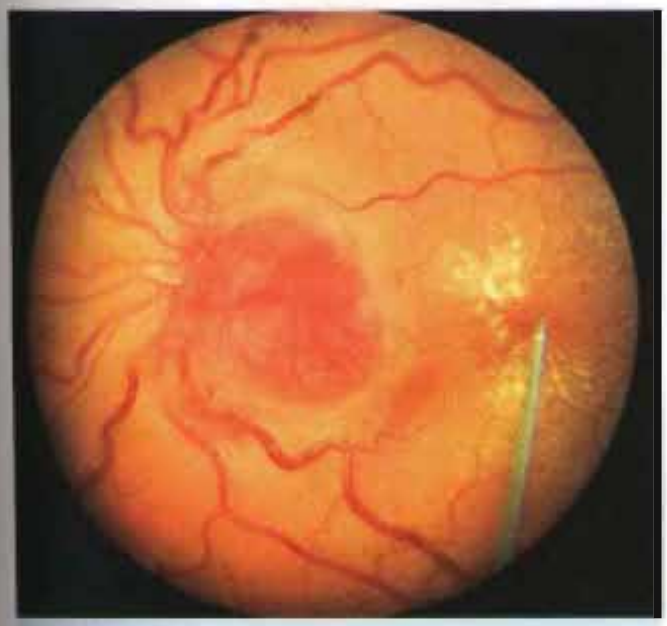

Fig. 11.85
Capillary haemangioma of the optic nerve head with macular exudates (Courtesy of K. Nischal)

Retinal cavernous haemangioma

Cavernous haemangioma of the retina or optic nerve head is a rare, congenital, unilateral, vascular hamartoma. A minority of patients have similar lesions of the skin and CNS. The combination is inherited in autosomal dominant fashion and is referred to as *neuro-oculocutaneous phaconatosis* or alternatively as *cavernoma multiplex*.

1. **Presentation** is in the second to third decades with vitreous haemorrhage, or more often as a chance finding.
2. **Signs** vary from a collection of aneurysms (Fig. 11.87) to an elaborate complex of vascular anomalies on the retina (Fig. 11.88) or optic nerve head (Fig. 11.89) which may rarely bleed (Fig. 11.90). Because of sluggish flow of blood, the red cells may sediment and separate from plasma, giving rise to 'menisci', or fluid levels within the lesion.
3. **Treatment** is generally not required although vitrectomy may be necessary in the rare event of non-absorbing vitreous haemorrhage.

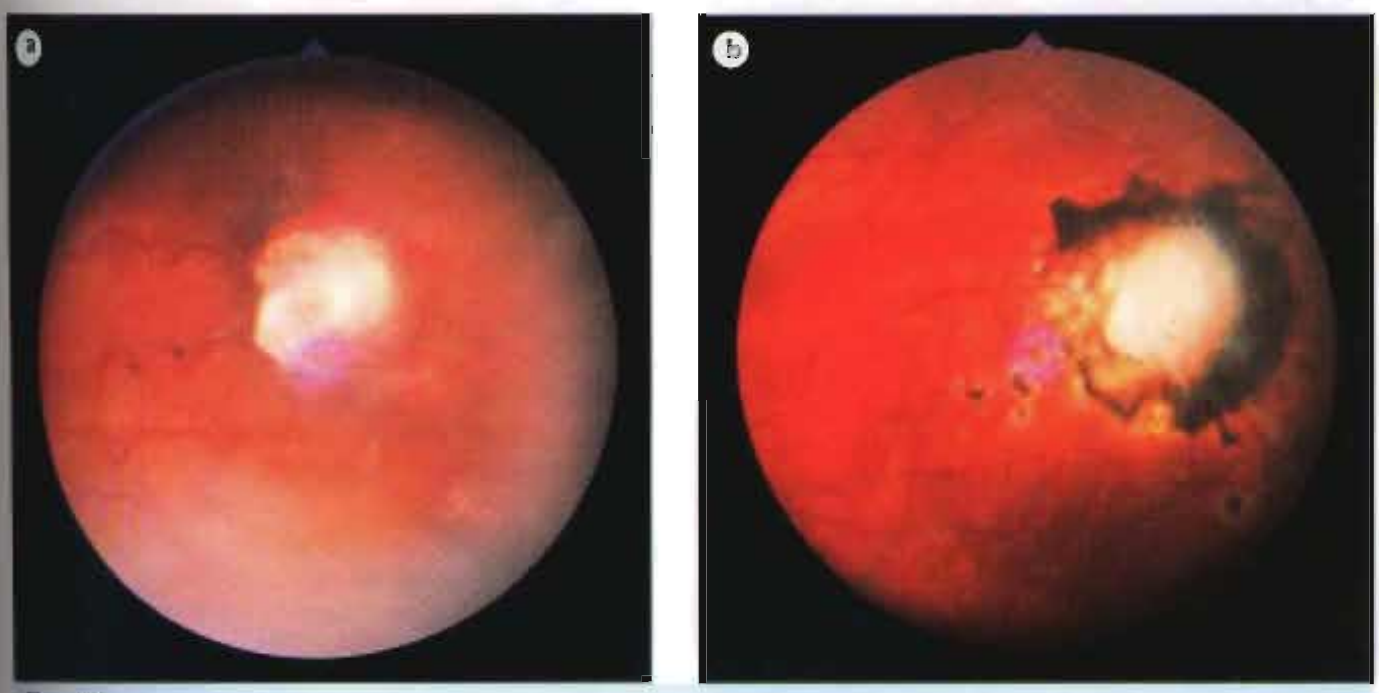

Fig. 11.86
(a) Retinal capillary haemangioma; (b) following laser photocoagulation

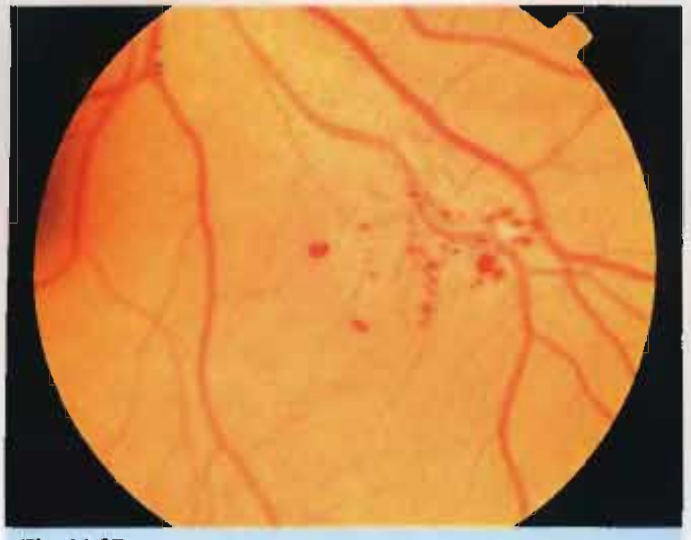

Fig. 11.87
Small retinal cavernous haemangioma (Courtesy of S. Milewski)

Fig. 11.90
Haemorrhage from retinal cavernous haemangioma

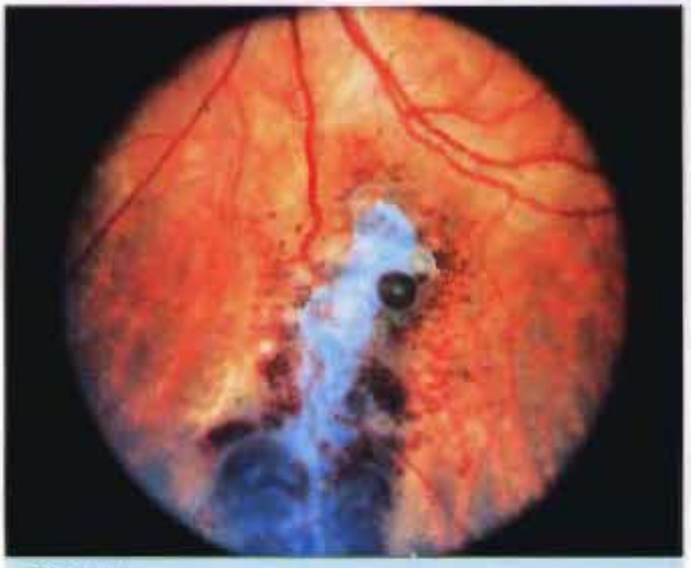

Fig. 11.88
Retinal cavernous haemangioma

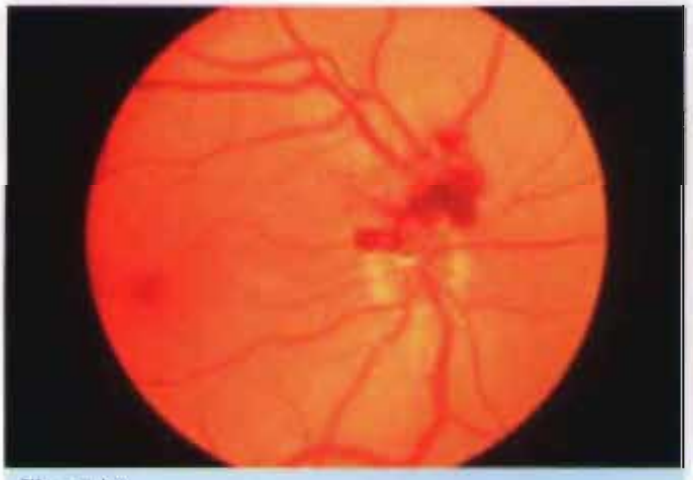

Fig. 11.89
Cavernous haemangioma of the optic nerve head (Courtesy of P. Morse)

Retinal racemose haemangioma

Racemose haemangioma of the retina and optic nerve head is a rare, usually unilateral, congenital arteriovenous malformation involving direct communication between the arteries and veins without an intervening capillary bed. Some patients have similar ipsilateral lesions involving the midbrain, basofrontal region and posterior fossa, an association which is referred to as the *Wyburn–Mason syndrome*. Brain involvement may lead to spontaneous haemorrhage or epilepsy. Occasionally, malformations may involve the maxilla, mandible and orbit. Facial skin lesions have also been reported.

1. **Presentation** may be with visual impairment or more commonly as a chance finding.
2. **Signs**. Enlarged, tortuous blood vessels which are often more numerous than in a normal fundus, with the vein and artery appearing similar (Fig. 11.91a).
3. **FA** shows absence of leakage (Fig. 11.91b–d) but very large lesions may occasionally lead to exudation and haemorrhage.
4. **Treatment** is not required.

Retinal vascular proliferative tumour

Retinal vasoproliferative tumour is a rare gliovascular lesion which occurs mostly in healthy individuals. It can be mistaken for a variety of other entities, most notably retinal angiomas, amelanotic choroidal melanomas and retinal telangiectasia.

1. **Presentation** is in the fifth to sixth decades with blurring of vision due to macular exudation.
2. **Signs**. A solitary, highly vascularized, yellow, retinal or subretinal mass with normal feeding and draining vessels (Fig. 11.92).
3. **Complications** include haemorrhage, exudation, cystoid macular oedema, epiretinal fibrosis and exudative retinal detachment.

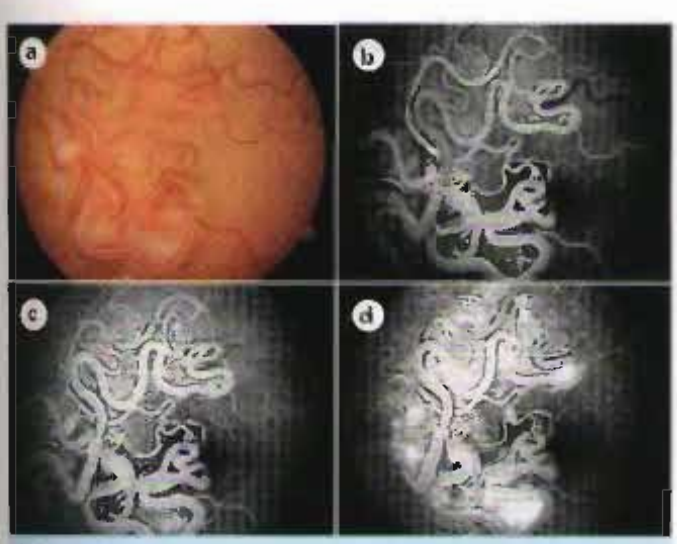

Fig. 11.91
(a) Retinal racemose haemangioma; (b–d) FA showing filling but no leakage (Courtesy of M. Karolczak-Kulesza)

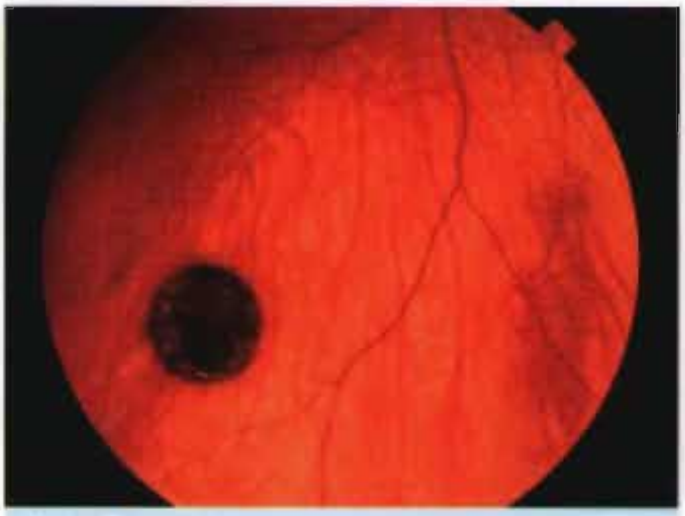

Fig. 11.93
Typical solitary congenital RPE hypertrophy with peripheral depigmentation

Fig. 11.92
Retinal vascular proliferative tumour (Courtesy of B. Damato)

Fig. 11.94
Typical solitary congenital RPE hypertrophy with hypopigmented central lacunae

4. **Treatment** with cryotherapy, laser photocoagulation or brachytherapy may be beneficial but the visual prognosis is guarded.

Tumours of the retinal pigment epithelium

Congenital hypertrophy of the retinal pigment epithelium

Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is a common benign lesion that may be (a) *typical*, which may be solitary or grouped, or (b) *atypical*. It is important to differentiate the two types because the latter has important systemic implications.

Typical CHRPE

1. Solitary

- A unilateral, flat, dark-grey or black, well-demarcated, round or oval lesion one to three disc diameters in size frequently with a hypopigmented rim just within the outer margin (Fig. 11.93).
- Depigmented lacunae which often enlarge or coalesce may be observed, particularly in older patients (Fig. 11.94).
- Some lesions may become depigmented with only a thin rim of residual pigment remaining at the margin (Fig. 11.95).

2. Grouped

- Usually unilateral, variably sized, sharply circumscribed, round, oval dark-grey or black lesions, often organized in a pattern simulating animal footprints (bear-track pigmentation) (Fig. 11.96).

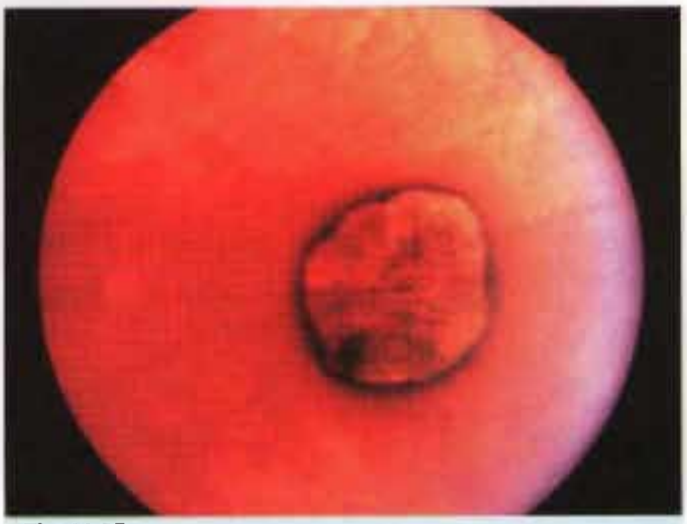

Fig. 11.95
Typical solitary congenital RPE hypertrophy which is nearly completely hypopigmented apart from a peripheral ring

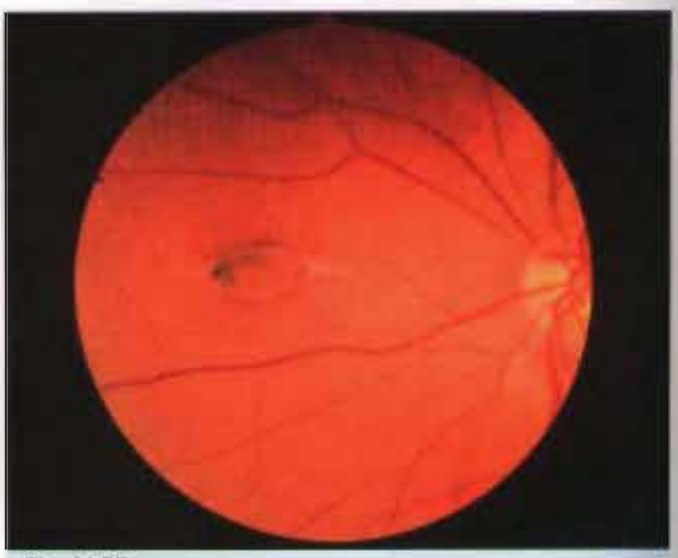

Fig. 11.97
Atypical congenital RPE hypertrophy (Courtesy of B. Jay)

Fig. 11.96
Typical grouped congenital RPE hypertrophy

Fig. 11.98
Intestinal adenomatous polyposis

- The lesions are often confined to one sector or quadrant of the fundus, with the smaller spots usually located more centrally.

Atypical CHRPE

1. Signs

- Multiple, bilateral, widely separated, frequently oval or spindle-shaped lesions of variable size associated with hypopigmentation at one margin (Fig. 11.97).
- The lesions have a haphazard distribution and may be pigmented, depigmented or heterogenous.

2. Systemic implications

*a. **Familial adenomatous polyposis*** (FAP) is a dominantly inherited condition characterized by adenomatous polyps throughout the rectum and colon which usually start to develop in adolescence (Fig. 11.98). If untreated, virtually all patients with FAP develop carcinoma of the colorectal region by the age of 50 years. From the age of 10 years, persons at risk should undergo regular endoscopic examinations and a prophylactic total colectomy should be performed early in adult life in all affected persons. As a result of the dominant inheritance pattern, intensive survey of family members is imperative. The FAP gene has been identified on 5q21–q22. Thus, molecular genetic analysis may identify carriers of the disease in selected cases. Over 80% of patients with FAP have atypical CHRPE which is present at birth. A positive criterion for FAP is the presence of at least four lesions whatever their size, or at least two lesions one of which must be large. Such fundus lesions in a family member should therefore arouse suspicion of FAP.

*b. **Gardner syndrome*** is characterized by FAP, osteomas of the skull and mandible and cutaneous soft tissue tumours such as epidermoid cysts, lipomas and fibromas.

*c. **Turcot syndrome*** is characterized by FAP and tumours of the CNS, particularly medulloblastoma and glioma.

Combined hamartoma of the retinal pigment epithelium and retina

Combined hamartoma of the RPE and retina is a rare, usually unilateral malformation which may be juxtapapillary or peripheral. It predominantly affects males and is found with increased frequency in patients with neurofibromatosis-2.

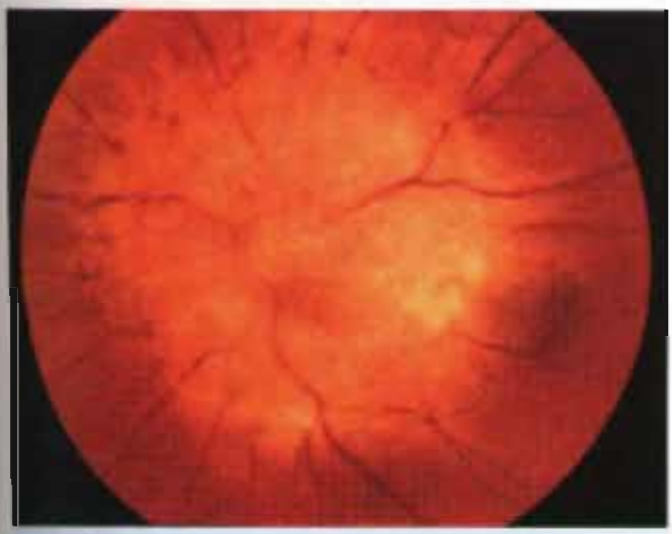

Fig. 11.99
Juxtapapillary combined hamartoma of the RPE and retina

Fig. 11.100
Distortion of the retina by a combined hamartoma of the RPE and retina

1. **Juxtapapillary**
   a. Presentation is in late childhood or early adulthood with blurred vision and metamorphopsia.
   b. Signs. Deep, slightly elevated, greyish-brown pigmentation associated with variable intra- and epiretinal gliosis, a fine network of dilated capillaries and vascular tortuosity (Fig. 11.99).
2. **Peripheral**
   a. Presentation is in early childhood with strabismus.
   b. Signs. A linear ridge associated with stretched blood vessels.
3. **Complications** include retinal and/or optic nerve head distortion (Fig. 11.100), macular oedema, choroidal neovascularization and, rarely, retinoschisis and retinal detachment.
4. **Treatment** of epiretinal membranes by vitreoretinal surgery may be tried but the visual results are often disappointing.

Hamartoma of the retinal pigment epithelium

This is an uncommon, small, jet-black lesion involving the RPE, often at the macula, which has a tendency to spill onto the surrounding inner retinal surface (Fig. 11.101).

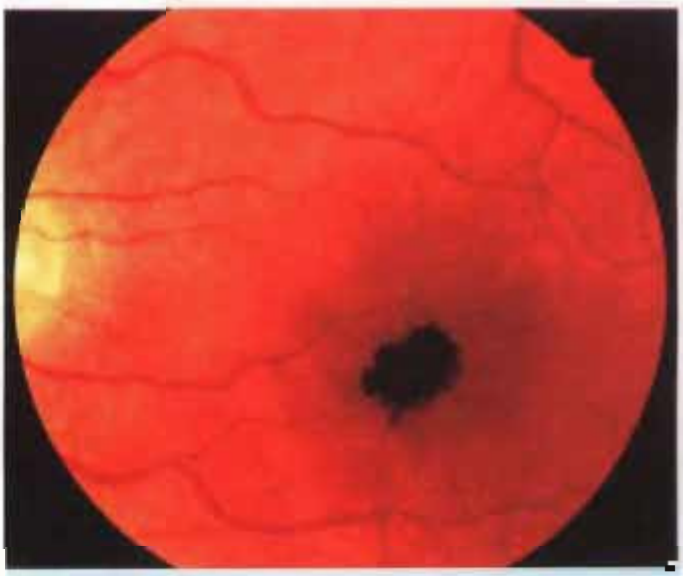

Fig. 11.101
Hamartoma of the RPE

CHAPTER 12

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Introduction

Definitions

Retinal detachment

A retinal detachment (RD) is a separation of the sensory retina from the retinal pigment epithelium (RPE) by subretinal fluid (SRF).

1. **Rhegmatogenous RD** (*rhegma*: break) occurs secondarily to a full-thickness defect in the sensory retina, which permits SRF derived from synchitic (liquefied) vitreous gel to gain access to the subretinal space.
2. **Non-rhegmatogenous RD** may be:
   a. ***Tractional***, in which the sensory retina is pulled away from the RPE by contracting vitreoretinal membranes; the source of SRF is unknown. Important causes include: proliferative diabetic retinopathy, retinopathy of prematurity, sickle cell retinopathy and penetrating posterior segment trauma.
   b. ***Exudative*** (serous, secondary), in which SRF derived from the choriocapillaris gains access to the subretinal space through damaged RPE. Important causes include choroidal tumours, exophytic retinoblastoma, Harada disease, posterior scleritis, subretinal neovascularization and severe hypertension.

Vitreoretinal traction

Vitreoretinal traction is a force exerted on the retina by structures originating in the vitreous and may be dynamic or static. The difference between the two is crucial to understanding the pathogenesis of the various types of RD.

1. **Dynamic** traction is induced by rapid eye movements and exerts a centripetal force towards the vitreous cavity. It is relevant to the pathogenesis of retinal tears and rhegmatogenous RD.
2. **Static** traction is independent of ocular movements and plays an important role in the pathogenesis of tractional RD and proliferative vitreoretinopathy. Static traction may be:
   a. ***Tangential*** (surface) which acts parallel to the surface of the retina as a result of contraction of epiretinal or subretinal membranes.
   b. ***Anteroposterior*** in which the retina is pulled anteriorly towards the vitreous base.
   c. ***Bridging*** (trampoline) in which traction occurs between one part of the retina and another, usually along the detached posterior hyaloid surface.

Retinal breaks

Retinal breaks are full-thickness defects of the sensory retina. They can be classified according to (a) *pathogenesis*, (b) *morphology* and (c) *location*.

Pathogenesis

1. **Tears** are caused by dynamic vitreoretinal traction. They have a predilection for the superior fundus (temporal more than nasal).
2. **Holes** are caused by chronic atrophy of the sensory retina and may be round or oval. They have a predilection for the temporal fundus (superior more than inferior) and are less dangerous than tears.

Morphology

Retinal tears may have one of five configurations:

1. **U-tears** (arrowhead tears) (Fig. 12.1a) consist of a flap, the apex of which is pulled anteriorly by the vitreous, the base remaining attached to the retina. The actual tear consists of two anterior extensions (horns), meeting at the apex, which points towards the posterior pole.
2. **Incomplete U-tears** may be linear (Fig. 12.1b), L-shaped (Fig. 12.1c) or J-shaped.
3. **Operculated tears** (Fig. 12.1d) in which the flap is completely avulsed by the detached vitreous gel.
4. **Dialyses** (Fig. 12.1e) are circumferential tears along the ora serrata with vitreous attachment to their posterior margins.

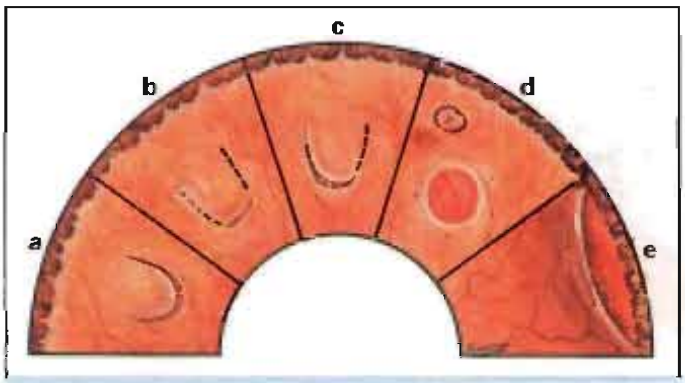

Fig. 12.1
Retinal tears. **(a)** U-shaped; **(b)** linear; **(c)** L-shaped; **(d)** operculated; **(e)** dialysis

Fig. 12.2
Giant retinal tear

5. **Giant tears** (Fig. 12.2) involve 90° or more of the circumference of the globe. They are a variant of U-shaped tears with the vitreous gel attached to the anterior margin of the break. Giant tears are most frequently located in the immediate post-oral retina and less commonly at the equator.

Location

1. **Oral** breaks are located within the vitreous base.
2. **Post-oral** breaks are located between the posterior border of the vitreous base and equator.
3. **Equatorial** breaks are at or near the equator.
4. **Post-equatorial** breaks are behind the equator.
5. **Macular** breaks, invariably holes, are at the macula.

Applied anatomy

Ora serrata

The ora is the junction between the retina and ciliary body (Fig. 12.3). The nasal ora is characterized by teeth-like extensions of retina onto the pars plana (dentate processes) separated by oral bays (Fig. 12.4). In the temporal ora the dentate processes are blunt or absent. Microcystoid degeneration is a normal finding involving the perioral retina characterized by tiny vesicles with indistinct boundaries which make the retina appear thickened and less transparent (Fig. 12.5). At the ora, fusion of the sensory retina with the RPE and choroid limits further forward extension of RD. However, there being no equivalent adhesion between the choroid and sclera, choroidal detachments invariably progress anteriorly to involve the ciliary body (ciliochoroidal

Fig. 12.4
Dentate processes and oral bays (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

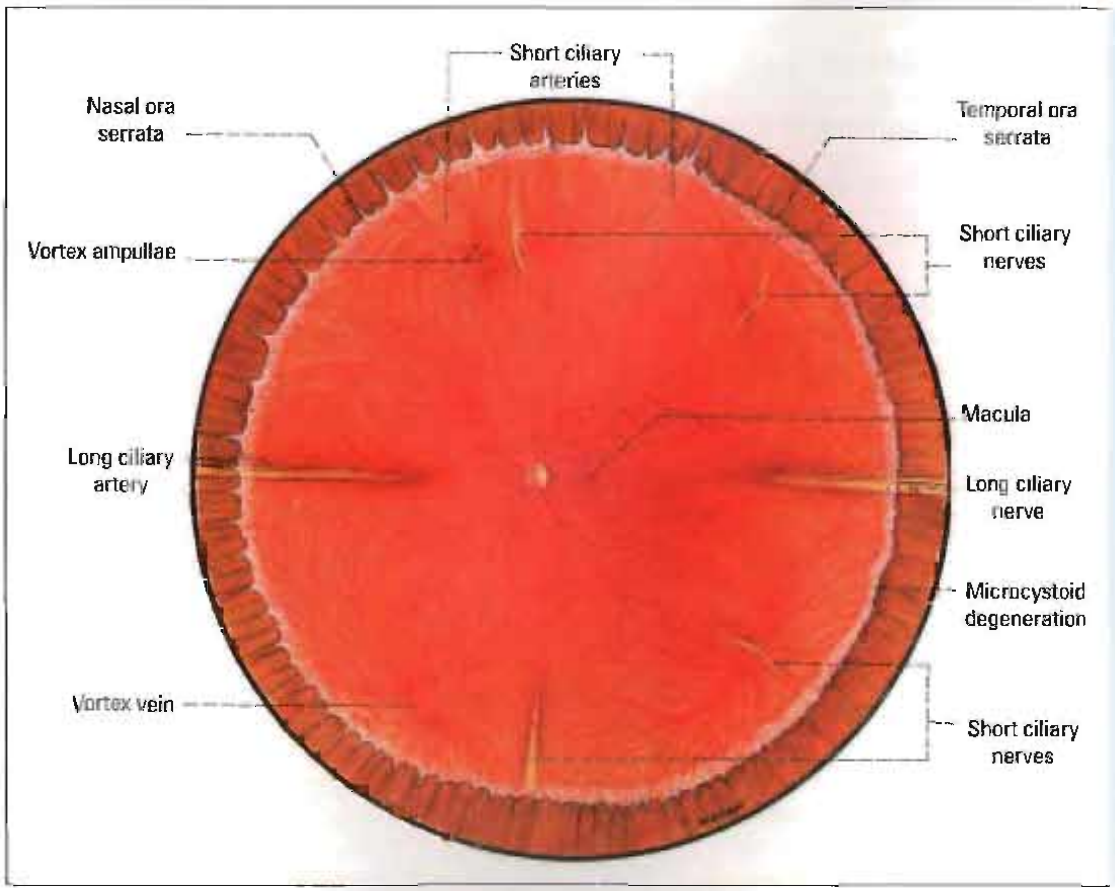

Fig. 12.3
Normal anatomical landmarks

Fig. 12.5
Microcystoid degeneration (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile. a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

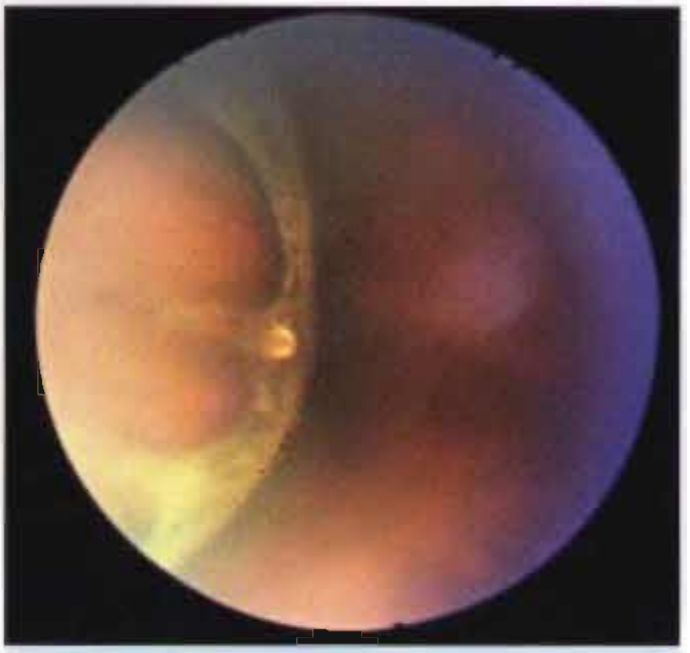

Fig. 12.7
Oral pearl (Courtesy of N.E Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California. 1982)

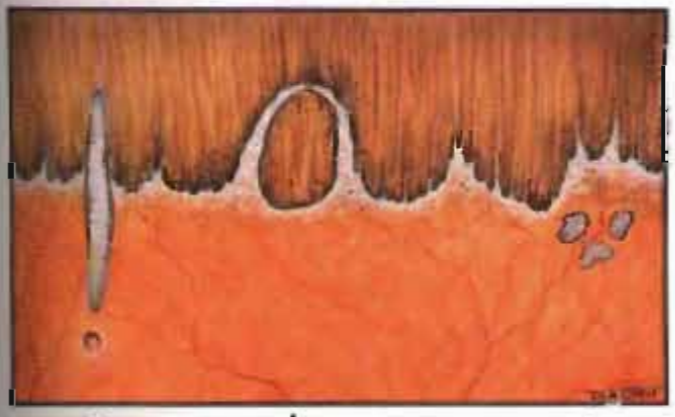

Fig. 12.6
Normal variants of the ora serrata. **(a)** Meridional fold with a small hole at its base; **(b)** enclosed oral bay; **(c)** granular tissue

detachment). The following congenital anomalies may occasionally have clinical significance (Fig. 12.6):

1. **A meridional fold** is a small radial fold of retina in line with a dentate process. It may occasionally exhibit a small retinal hole at its base (Fig. 12.6a).
2. **An enclosed oral bay** is a small island of pars plana surrounded by retina as a result of meeting of two adjacent dentate processes (Fig. 12.6b). It should not be mistaken for a retinal hole because it is located anterior to the ora serrata.
3. **Granular tissue** characterized by multiple, tiny, white opacities within the vitreous base (Fig. 12.6c) can sometimes be mistaken for very small peripheral opercula.
4. **Oral pearls** (Fig. 12.7) are uncommon tiny white lesions.

Vitreous base

This is a 3–4 mm wide zone straddling the ora serrata (Fig. 12.8). The cortical vitreous is strongly adherent at the vitreous base, so that following acute posterior vitreous detachment (PVD) the posterior hyaloid surface remains attached to the posterior border of the vitreous base. Pre-existing perioral retinal holes within the vitreous base therefore do not lead to RD.

Vitreoretinal adhesions

1. **Normal adhesion** between the cortical vitreous and the internal limiting membrane is fairly loose, except at the following sites:
   - At the vitreous base (very strong).
   - Around the optic disc margin (fairly strong).
   - Around the fovea (weak).
   - Around peripheral retinal blood vessels (usually weak).
2. **Abnormal adhesions** may occasionally be associated with retinal tear formation caused by dynamic vitreo-retinal traction in eyes with acute PVD. They occur at the following sites:
   - Posterior border of lattice degeneration.
   - Congenital cystic retinal tufts which are white, ovoid, inward projections of sensory retina located in the post-oral area (Fig. 12.9).
   - Retinal pigment clumps.
   - Peripheral paravascular condensations.
   - Vitreous base anomalies such as posterior tongue-like extensions and isolated islands.
   - Areas of 'white-without-pressure'.

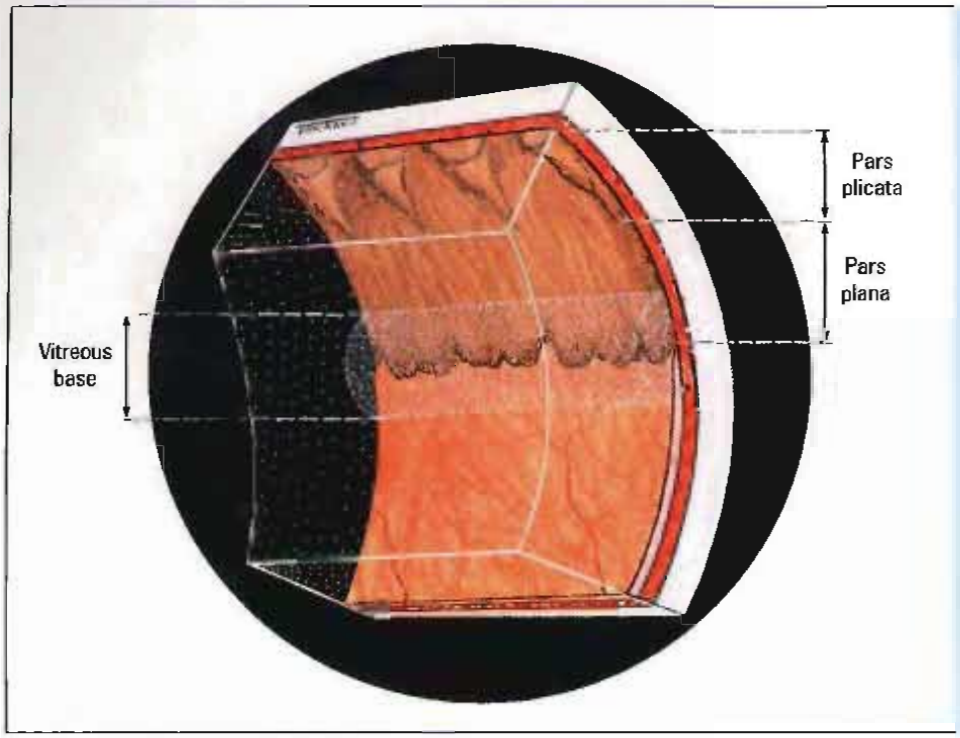

Fig. 12.8
Anatomy of the vitreous base

Fig. 12.9
Cystic retinal tuft (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence, California, 1982)

Blood vessels

1. **The long posterior ciliary arteries** (accompanied by corresponding nerves) are recognized as yellow lines that start behind the equator and run anteriorly in the 3 and 9 o'clock meridians (*see* Fig. 12.3). They divide the fundus into upper and lower zones. The arteries run in the suprachoroidal space in line with the horizontal recti.
2. **The short posterior ciliary arteries** are unaccompanied by nerves and may be difficult to identify ophthalmoscopically. The short ciliary nerves appear as peripheral radial yellow lines.
3. **The vortex ampullae** are located just posterior to the equator in the 1, 5, 7 and 11 o'clock meridia. Externally the vortex veins emerge from their scleral canals at variable distances from the equator. They limit posterior extension of a choroidal detachment as they pass through the suprachoroidal space into their scleral canals.

Examination techniques

Indirect ophthalmoscopy

Condensing lenses of various powers and diameters are available (Fig. 12.10). The higher the power, the lower the magnification, the shorter the working distance but the greater the field of view. The technique is as follows:

1. Both pupils should be well dilated.
2. The patient should ideally be supine.
3. The lens is held with the flat surface facing the patient and should be held parallel to the patient's iris plane at all times.
4. The red reflex and then the fundus are located.
5. The tendency to move towards the patient should be avoided if difficulty in visualizing the fundus is encountered.
6. The patient is asked to move the eyes and head into optimal positions for examination.

Fig. 12.10
Condensing lenses used for indirect ophthalmoscopy

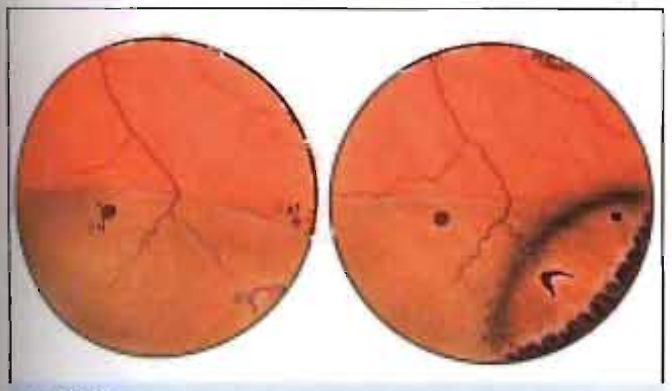

Fig. 12.11
(Left) Retinal breaks in detached retina without scleral indentation; (right) with scleral indentation

Fig. 12.13
Mound created by scleral indentation (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

Scleral indentation

Purpose

Scleral indentation enhances visualization of the peripheral retina anterior to the equator and enables a dynamic fundus examination to be performed. For example, Fig. 12.11 (left) shows a retinal hole (a) near the equator, visible without scleral indentation because the underlying choroid provides good contrast and the hole appears red. However, a small round hole (b) near the ora serrata or a small U-tear (c) near the posterior border of the vitreous base may be overlooked without scleral indentation. Figure 12.11 (right) shows that with scleral indentation the small hole (b) is seen more easily because the contrast between choroid and sensory retina is enhanced. Indentation also brings the peripheral fundus into view and enables the flap of the small U-tear (c) to be seen in profile.

Technique

1. To view the ora serrata at 12 o'clock, the patient is asked to look down. The scleral indentor is applied to the outside

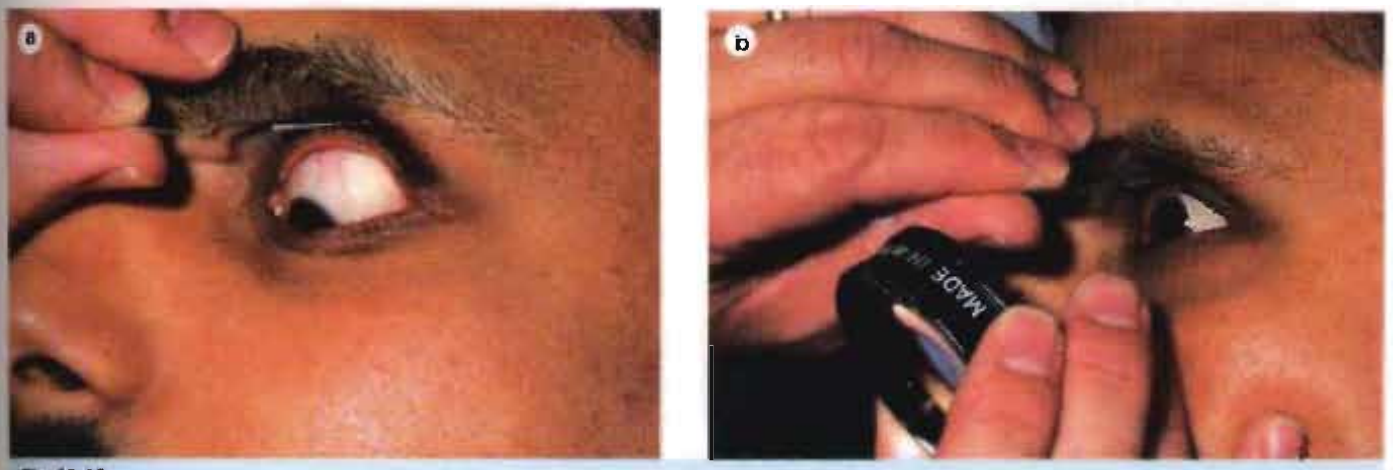

Fig. 12.12
(a) Insertion of an unfolded paper clip; (b) scleral indentation

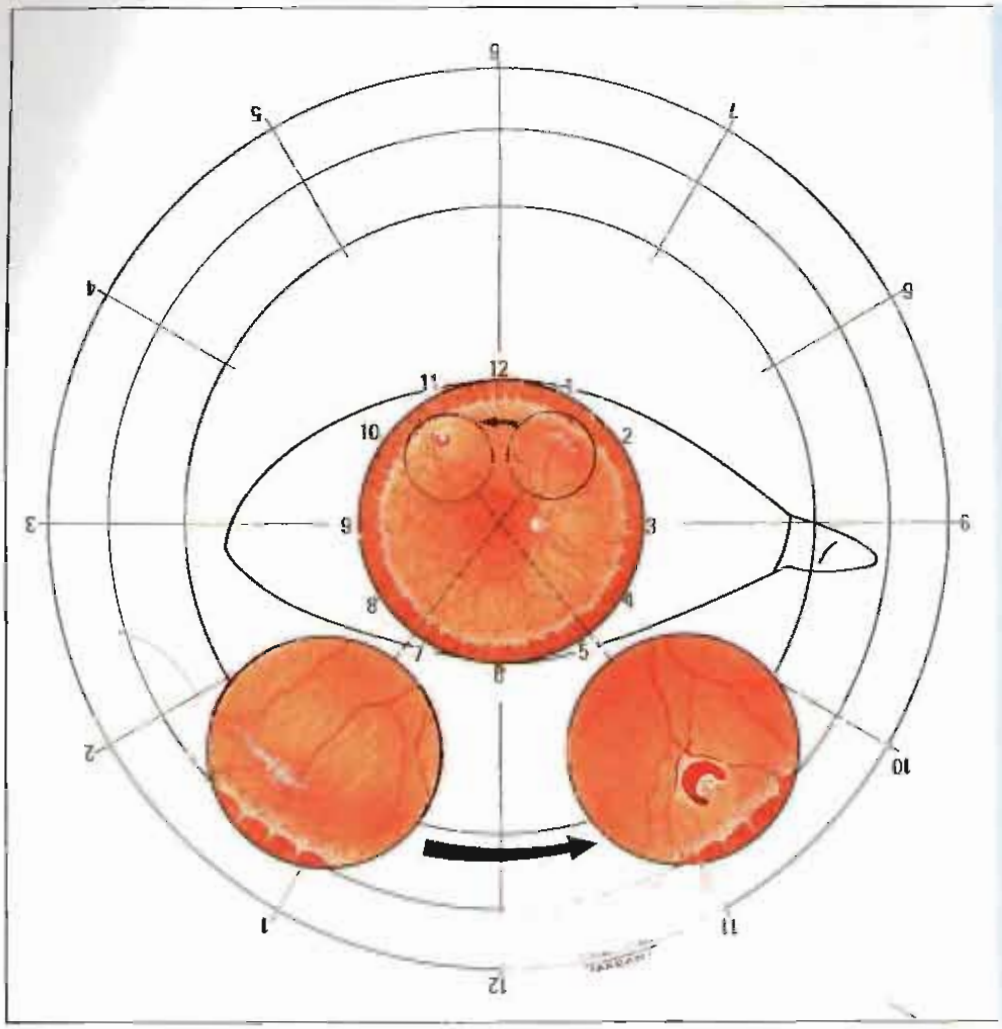

Fig. 12.14
Technique of drawing retinal lesions (see text)

of the upper eyelid at the margin of the tarsal plate (Fig. 12.12a).

2. With the indentor in place, the patient is asked to look up: the indentor is simultaneously advanced into the anterior orbit parallel with the globe (Fig. 12.12b).
3. The examiner's eyes should be aligned with the condensing lens and the indentor, with which gentle pressure is exerted. The indentation is observed as a mound in the fundus (Fig. 12.13). The indentor should be maintained tangential to the globe because perpendicular indentation is uncomfortable.
4. The indentor is moved to adjacent parts of the fundus, ensuring that the examiner's eyes, condensing lens and indentor are all in a straight line.

Fundus drawing

1. **Technique.** Because the image seen with the indirect ophthalmoscope is vertically inverted and laterally reversed, the top of the chart is placed towards the patient's feet (upside down). In this way the inverted position of the chart in relation to the patient's eye corresponds to the inverted image of the fundus. For example (Fig. 12.14), a 1-clock at

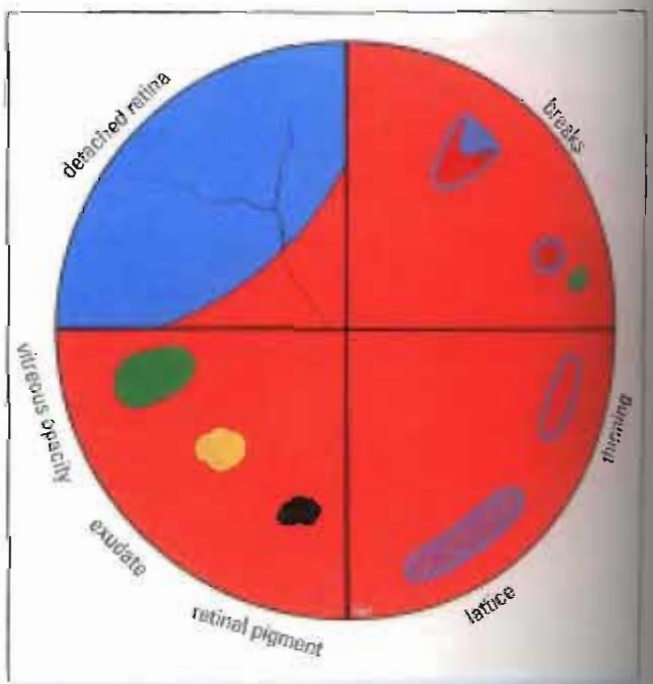

Fig. 12.15
Colour code for retinal drawing

11 o'clock in the eye will correspond to the 11 o'clock position on the chart. The same applies to the area of lattice degeneration between 1 and 2 o'clock.

2. **Colour code** (Fig. 12.15)
   - The boundaries of the RD are delineated, starting at the optic disc and then extending to the periphery.
   - Detached retina is drawn in blue and flat retina in red.
   - Retinal veins are drawn in blue but arteries are not drawn.
   - Retinal breaks are drawn in red with blue outlines; the flap of a retinal tear is drawn in blue.
   - Thin retina is indicated by red hatchings outlined in blue; lattice degeneration is shown as blue hatchings outlined in blue; retinal pigment as black; retinal exudates yellow; and vitreous opacities (including blood) green.

Goldmann triple-mirror examination

Goldmann triple-mirror

This consists of four parts (Fig. 12.16):

1. **The central part** provides a 30° view of the posterior pole.
2. **The equatorial mirror** (largest and oblong shaped) enables visualization from 30° to the equator.
3. **The peripheral mirror** (intermediate in size and square shaped) enables visualization between the equator and the ora serrata.
4. **The gonioscopic mirror** (smallest and dome shaped) may be used for visualizing the extreme retinal periphery and pars plana. It is therefore apparent that the smaller the mirror the more peripheral the view.

NB: The central part affords an upright virtual image of the posterior pole. With regard to the three mirrors:

- The mirror should be positioned opposite the area of the fundus to be examined.

Fig. 12.16
Goldmann triple-mirror

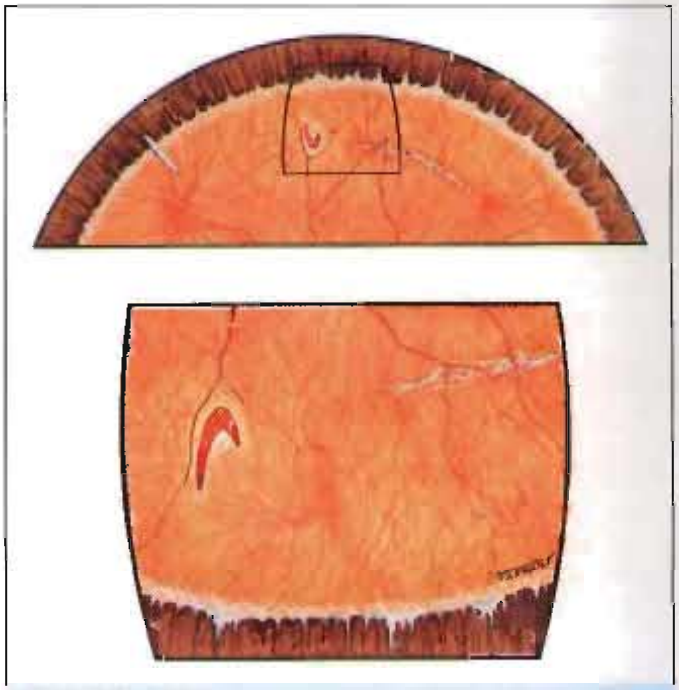

Fig. 12.17
(Top) U-tear left of 12 o'clock and an island of lattice degeneration right of 12 o'clock; **(bottom)** same lesions seen with the triple mirror positioned at 6 o'clock

- When viewing the vertical meridian, the image is upside down (Fig. 12.17).
- When viewing the horizontal meridian, the image is laterally reversed.

Fig. 12.18
Illumination column tilted and positioned right of centre to view the oblique meridians at 1.30 o'clock and 7.30 o'clock

Technique

1. The contact lens is inserted as for gonioscopy (*see* Chapter 9).
2. The illumination column should always be tilted (Fig. 12.18) except when viewing the vertical meridia.
3. When viewing sectors of the peripheral retina the axis of the beam is rotated so that it is always at right angles to the mirror.
4. To visualize the entire fundus the lens is rotated 360° using first the equatorial mirror and then the peripheral mirror.
5. To obtain a more peripheral view of any given sector the lens is tilted to the opposite side and the patient asked to move the eyes to the same side. For example, to obtain a more peripheral view of the 12 o'clock meridian (mirror at 6 o'clock) the lens is tilted down and the patient looks up.
6. The vitreous cavity is viewed through the central lens using both a horizontal and a vertical slit beam, and the posterior pole is then examined.

Fig. 12.19
Posterior vitreous detachment

Indirect slit-lamp biomicroscopy

This method utilizes high-power lenses (commonly +90 D and +78 D) designed to obtain a wide field of view. The lenses are used in a similar manner to an ordinary indirect ophthalmoscope lens and the image is likewise vertically inverted and laterally reversed.

Technique

1. The slit beam is adjusted to about one-quarter its full round diameter.
2. The illumination angle is set coaxially with the slit-lamp viewing system.
3. The lens is interposed in the slit beam immediately in front of the patient's eye (*see* Fig. 13.6).
4. The red reflex is identified, following which the microscope is pulled back, until the fundus comes into view.
5. The fundus is scanned, executing horizontal and vertical adjustment of the slit-lamp, while holding the lens still.
6. The width of the beam may be increased to obtain a larger field of view.
7. The magnification may be increased for greater detail as necessary.
8. To visualize peripheral retina the patient is asked to assume appropriate positions of gaze as with standard indirect ophthalmoscopy.

Fig. 12.20
Weiss ring (Courtesy of V. Tanner)

Interpretation of findings

- The normal vitreous in a young individual appears homogeneous with the same density throughout.
- The central vitreous cavity may contain optically empty spaces (lacunae). The condensed lining of a large cavity may be mistaken for a detached posterior hyaloid surface (pseudo-PVD).
- In eyes with PVD the detached posterior hyaloid surface can be seen (Fig. 12.19).
- A Weiss ring (Fig. 12.20) is an annular opacity representing a ring of glial tissue detached from the margin of the optic disc: it is virtually pathognomonic of PVD.
- Pigment cells ('tobacco dust') in the anterior vitreous in a patient complaining of sudden onset of flashing lights and floaters are strongly suggestive of a retinal tear (Fig. 12.21). A careful examination of the peripheral retina (particularly superiorly) is mandatory. The cells represent macrophages containing shed RPE cells.
- Numerous small opacities within the anteriorly displaced gel or in the retrohyaloid space are strongly suggestive of blood.

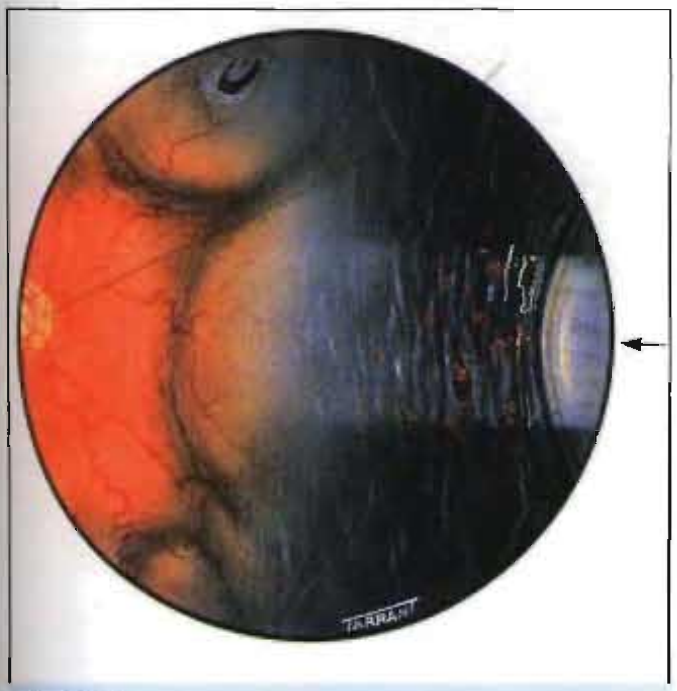

Fig. 12.21
Retinal detachment with a superior U-tear and tobacco dust

- Because of the wide field of view it may also be possible to visualize equatorial retinal tears.

Finding the primary retinal break

The primary break is the one deemed responsible for the RD, although further (secondary) breaks may also be present. Identifying the primary break is of paramount importance and aided by the following considerations.

Quadrantic distribution

- About 60% are in the upper temporal quadrant.
- About 15% are in the upper nasal quadrant.
- About 15% are in the lower temporal quadrant.
- About 10% are in the lower nasal quadrant.

The upper temporal quadrant is therefore by far the most common site for retinal break formation and should be examined in great detail if a break cannot be detected initially.

> ***NB:*** About 50% of eyes with RD have more than one break; and in most cases these are located within 90° of each other.

Configuration of retinal detachment

SRF usually spreads in a gravitational fashion. The configuration of an RD is governed by anatomical limits (ora serrata and optic disc) and the location of the primary retinal break. If the primary break is located superiorly, the SRF first gravitates inferiorly on the same side as the break and then ascends on the opposite side. The likely location of the primary retinal break can therefore be predicted by analysing the configuration of the RD (Fig. 12.22).

- A shallow inferior RD in which the SRF is slightly higher on the temporal side points to a primary break on that side (Fig. 12.22a).
- A primary break located at 6 o'clock will cause an inferior RD with equal fluid levels (Fig. 12.22b).
- In a bullous inferior RD the primary break usually lies above the horizontal meridian (Fig. 12.22c).
- If the primary break is located in the upper nasal quadrant the SRF will revolve around the optic disc and then rise

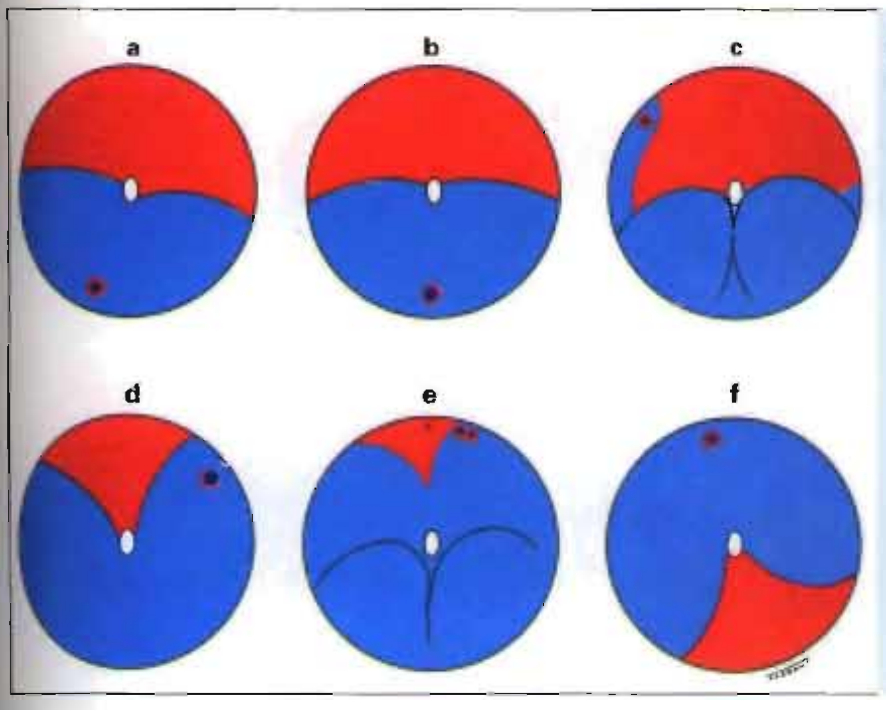

Fig. 12.22
Distribution of subretinal fluid in relation to the primary break

on the temporal side until level with the primary break (Fig. 12.22d).

- A subtotal RD with a superior wedge of attached retina points to a primary break located in the periphery nearest its highest border (Fig. 12.22e).
- When the SRF crosses the vertical midline above, the primary break is near 12 o'clock, the lower edge of the RD corresponding to the side of the break (Fig. 12.22f).

NB: Diligent observation of the aforementioned principles prevents the treatment of secondary breaks while overlooking the primary break. Ensuring that the labelling of a break as 'primary' conforms to the configuration of the RD is therefore essential.

History

Although the quadrantic location of light flashes (photopsia) is of no value in predicting the location of the primary break, the quadrant in which the visual field defect first appeared may be of considerable value, since it corresponds to the area where the RD originated. For example, if the field defect started in the upper nasal quadrant the primary break is probably located in the lower temporal quadrant.

Ultrasonography

B-scan ultrasonography is useful in eyes with opaque media suspected of harbouring a retinal tear or RD. This applies particularly in the context of recent dense vitreous haemorrhage precluding visualization of the fundus. Under these circumstances ultrasonography may help to differentiate PVD (Fig. 12.23) from RD (Fig. 12.24). It may also be possible to detect the presence of a retinal tear in flat retina (Fig. 12.25). Dynamic ultrasonography, in which examination of intraocular structures is performed during lateral eye movements, is helpful in assessing the mobility of the

Fig. 12.23
Axial B-scan ultrasound showing intragel haemorrhage and posterior vitreous detachment (Courtesy of K. Nischal)

Fig. 12.24
Sagittal B-scan ultrasound showing inferior retinal detachment (Courtesy of K. Nischal)

Fig. 12.25
Sagittal B-scan ultrasound showing a superior retinal tear associated with posterior vitreous detachment but a flat retina (Courtesy of K. Nischal)

Fig. 12.26
Sagittal B-scan ultrasound showing total retinal detachment associated with advanced proliferative vitreoretinopathy (triangular sign) (Courtesy of K. Nischal)

vitreous and retina in eyes with proliferative vitreoretinopathy (Fig. 12.26).

Pathogenesis of rhegmatogenous retinal detachment

Rhegmatogenous RD affects about 1:10,000 of the population each year and both eyes are eventually involved in about 10% of cases. The retinal breaks responsible for RD are caused by interplay between (a) *dynamic vitreoretinal traction* and (b) *predisposing degeneration* in the peripheral retina. Myopia may also play a significant role.

Dynamic vitreoretinal traction

Pathogenesis

Synchysis is a liquefaction of the vitreous gel (Fig. 12.27a). Some eyes with synchysis develop a hole in the thinned posterior vitreous cortex which overlies the fovea. Synchytic

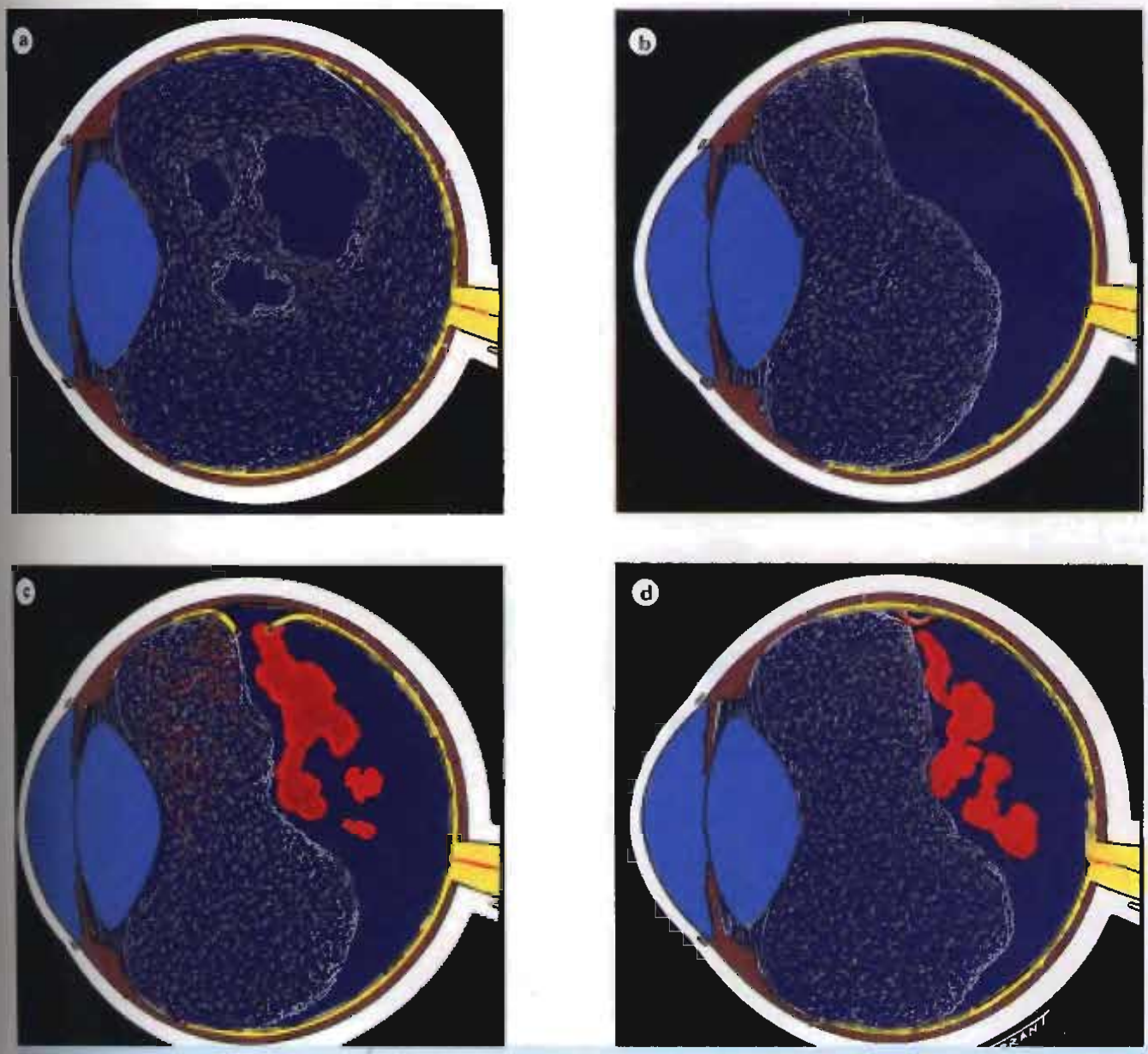

Fig. 12.27
(a) Synchysis; (b) uncomplicated posterior vitreous detachment; (c) retinal tear formation and vitreous haemorrhage; (d) avulsion of retinal blood vessel and vitreous haemorrhage

fluid from within the centre of the vitreous cavity passes through this defect into the newly formed retrohyaloid space. This process hydro-dissects the posterior vitreous surface from the internal limiting membrane (ILM) of the sensory retina as far forward as the posterior border of the vitreous base. The remaining solid vitreous gel collapses inferiorly and the retrohyaloid space is occupied entirely by synchytic fluid. This process is called acute rhegmatogenous PVD with collapse and will be referred to as acute PVD henceforth. The incidence of acute PVD increases with age and myopia.

Complications of acute PVD

These are dependent on the strength and extent of pre-existing vitreoretinal adhesions.

1. **No complications** (Fig. 12.27b) occur in most eyes, since vitreoretinal attachments are weak.
2. **Retinal tears** develop in about 10% of eyes as a result of traction at sites of abnormally strong vitreoretinal adhesions. Tears associated with acute PVD are usually symptomatic, U-shaped, located in the upper fundus (Fig. 12.28) and frequently associated with vitreous haemorrhage resulting from rupture of peripheral retinal blood vessels (*see* Fig. 12.27c). After a tear has formed, the synchytic retrohyaloid fluid has direct access to the subretinal space and unless the tear is treated prophylactically by photocoagulation or cryotherapy the risk of RD is high.
3. **Avulsion** of a peripheral retinal blood vessel resulting in vitreous haemorrhage in the absence of retinal tear formation (*see* Fig. 12.27d).

Predisposing peripheral retinal degenerations

About 60% of all breaks develop in areas of the peripheral retina that manifest specific changes. These lesions may be associated with spontaneous breakdown of pathologically thin retinal tissue to cause a retinal hole, or may predispose to retinal tear formation in eyes with acute PVD. Retinal holes are usually smaller than tears and carry a lower risk of RD.

Lattice degeneration

This is present in about 8% of the general population and in about 40% of eyes with RD. It is an important cause of RD in young myopes. Lattice-like lesions are frequently found in patients with Marfan syndrome, Stickler syndrome and Ehlers–Danlos syndrome, all of which are associated with an increased risk of RD.

1. **Signs**
   a. ***Typical*** lattice consists of sharply demarcated, circumferentially orientated, spindle-shaped areas of retinal thinning (Fig. 12.29), most frequently located between the equator and the posterior border of the vitreous base. Lattice is characterized by discontinuity of the internal limiting membrane, with variable atrophy of the underlying sensory retina. The lesions are usually bilateral and more often located in the temporal than nasal half of the fundus, and superiorly rather than inferiorly. A characteristic feature is an arborizing network of tiny white lines within the islands which may be associated with retinal pigment epithelial

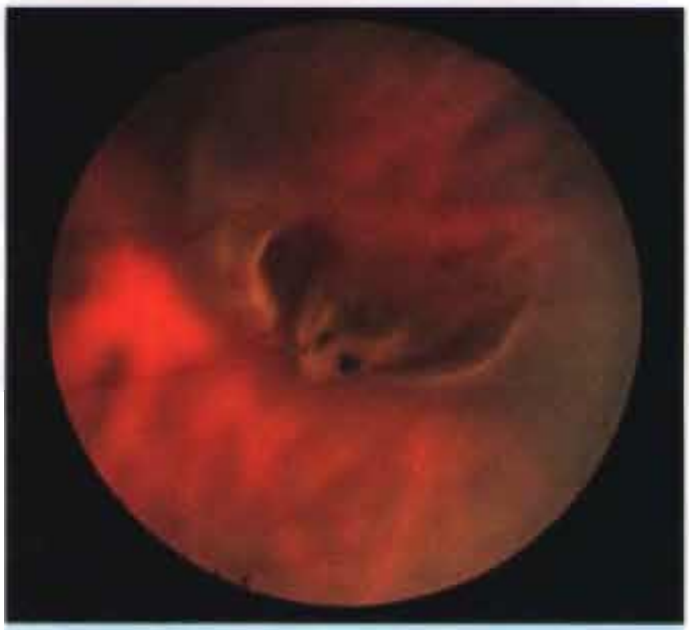

Fig. 12.28
Superior U-shaped tear associated with acute posterior vitreous detachment. (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*, Criterion Press, Torrence California, 1982)

Fig. 12.29
Lattice degeneration forming a shallow crater (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*, Criterion Press, Torrence, California, 1982)

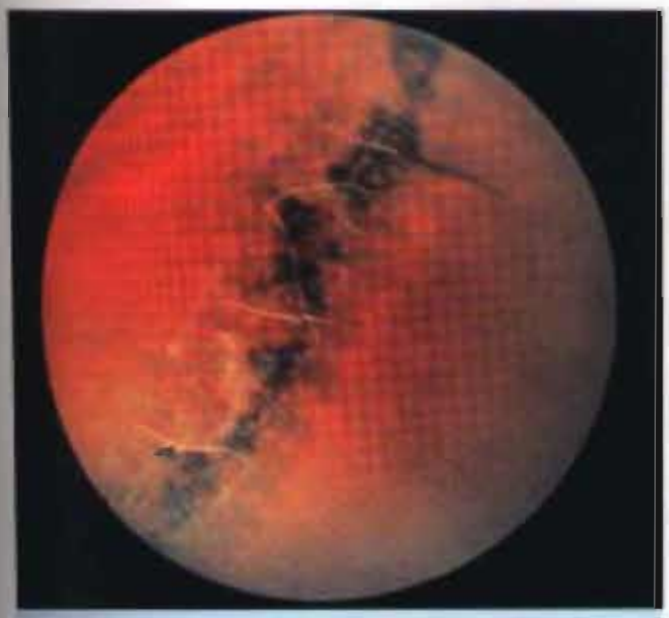

Fig. 12.30
Lattice degeneration with white lines and retinal pigment epithelial changes

Fig. 12.32
Vitreous changes associated with lattice degeneration

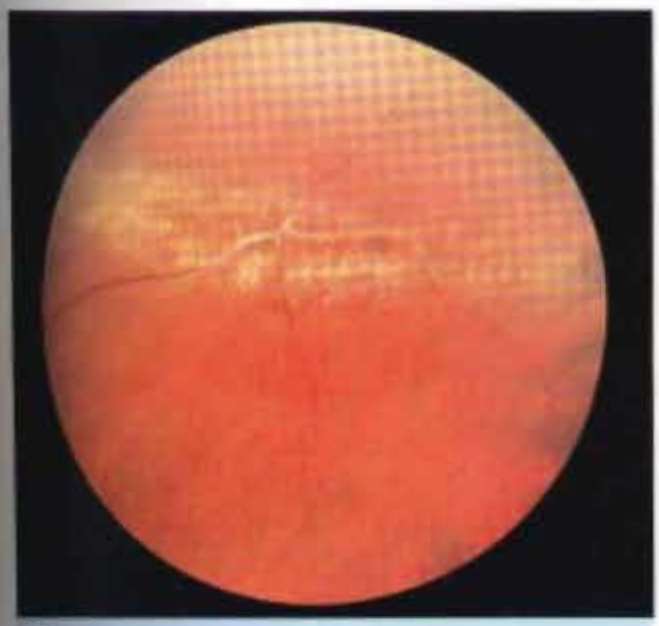

Fig. 12.31
Lattice degeneration with snowflakes (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

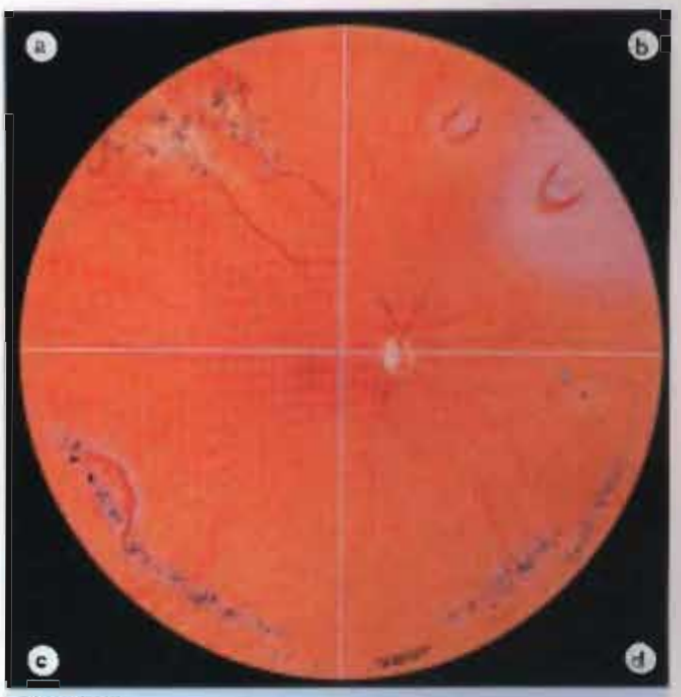

Fig. 12.33
(a) Atypical radial lattice degeneration; (b) lattice degeneration on the flap of a U-tear; (c) tractional tear along the posterior margin of lattice degeneration; (d) small round holes in lattice degeneration

changes (Fig. 12.30). Some lattice lesions may be associated with 'snowflakes' (remnants of degenerate Müller cells) (Fig. 12.31). The vitreous overlying an area of lattice is synchytic but the vitreous attachments around the margin of the lesion are exaggerated (Fig. 12.32).

b. *Atypical* lattice is characterized by radially orientated lesions continuous with peripheral blood vessels which may extend posterior to the equator (Fig. 12.33a). This type typically occurs in patients with Stickler syndrome.

2. Complications

- No complications are encountered in most patients, even in the presence of small holes which are frequently found within islands of lattice (Fig. 12.34, *see* Fig. 12.33d).

Fig. 12.34
Holes within lattice degeneration (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

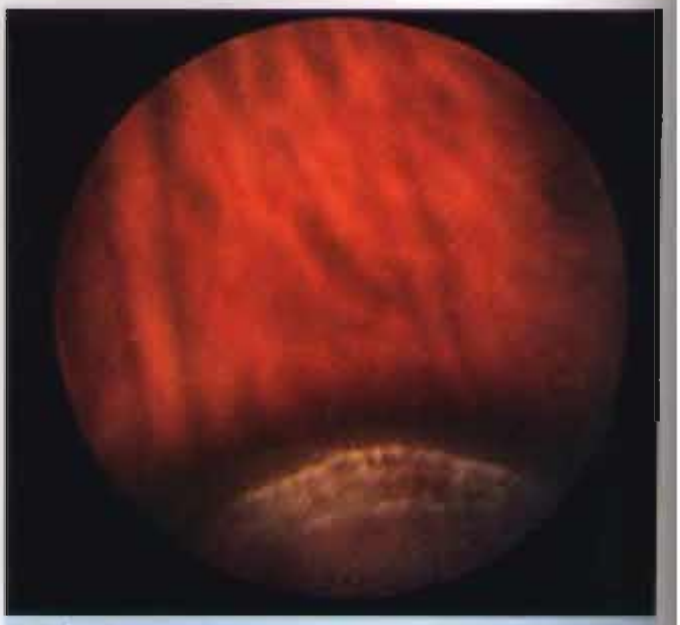

Fig. 12.36
Snailtrack degeneration seen on scleral indentation (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

Fig. 12.35
Large tear associated with lattice degeneration (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

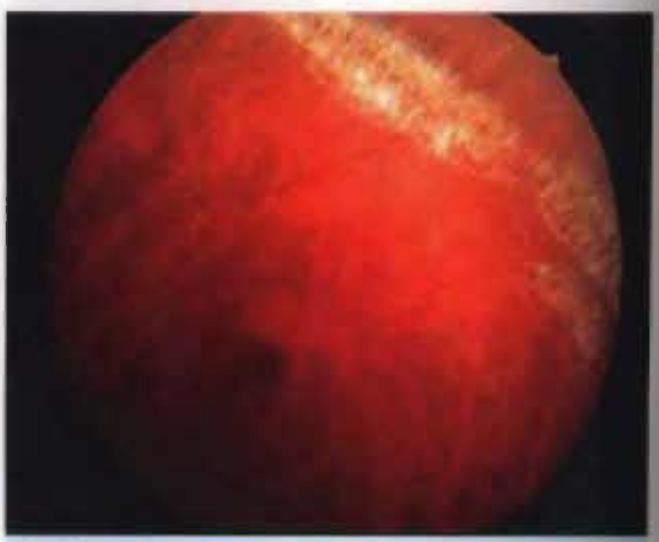

Fig. 12.37
Holes within snailtrack degeneration

NB: RD associated with atrophic holes may occasionally occur, particularly in young myopes. In these patients it may not be preceded by symptoms of acute PVD (photopsia and floaters) and the SRF usually spreads slowly.

- RD due to tractional tears may occur in eyes with acute PVD (Fig. 12.35). Tractional tears typically develop along the posterior edge of an island of lattice (*see* Fig. 12.33c) as a result of dynamic traction at the site of tenacious vitreoretinal attachment. Occasionally a small island of lattice may be seen on the flap of a retinal tear (*see* Fig. 12.33b).

Snailtrack degeneration

1. **Signs**. Sharply demarcated circumferentially oriented bands of tightly packed 'snowflakes', which give the peripheral retina a white frost-like appearance. They are usually longer than islands of lattice (Fig. 12.36). Although snailtrack degeneration is associated with overlying vitreous liquefaction, marked vitreous traction at the posterior border of the lesions is seldom present, so that tractional U-tears rarely occur.
2. **Complications** include hole formation (Fig. 12.37) which may result in RD.

Degenerative retinoschisis

Retinoschisis is a splitting of the sensory retina into two layers: an outer (choroidal layer) and an inner (vitreous layer). The two main types are (a) *degenerative* and (b) *congenital* (*see* Chapter 15). Degenerative retinoschisis is present in about 5% of the population over the age of 20 years and is particularly prevalent in hypermetropes (70% of patients are hypermetropic) and is nearly always asymptomatic.

1. Classification

a. ***Typical***, in which the split occurs at the outer plexiform layer.

b. ***Reticular***, which is less common, in which the split is at the level of the nerve fibre layer.

2. Signs

- Early changes usually involve the extreme inferotemporal periphery of both fundi, appearing as an exaggeration of microcystoid degeneration with a smooth elevation of the retina (Fig. 12.38).
- Progression may occur circumferentially until the entire fundus periphery is involved. The typical type usually remains anterior to the equator although the reticular type may spread beyond the equator (Fig. 12.39).
- The surface of the inner layer may show 'snowflakes' as well as sheathing or 'silver-wiring' of blood vessels and the schisis cavity may be bridged by torn grey-white tissue (Fig. 12.40).
- The outer layer has a beaten-metal appearance and shows the phenomenon of 'white-with-pressure'.

> ***NB:*** Unlike RD, retinoschisis is immobile.

3. Complications

- No complications occur in most cases and the condition is innocuous.

Fig. 12.38
Circumferential microcystoid degeneration and degenerative retinoschisis in the inferotemporal and superotemporal quadrants

Fig. 12.39
Degenerative retinoschisis extending posterior to the equator

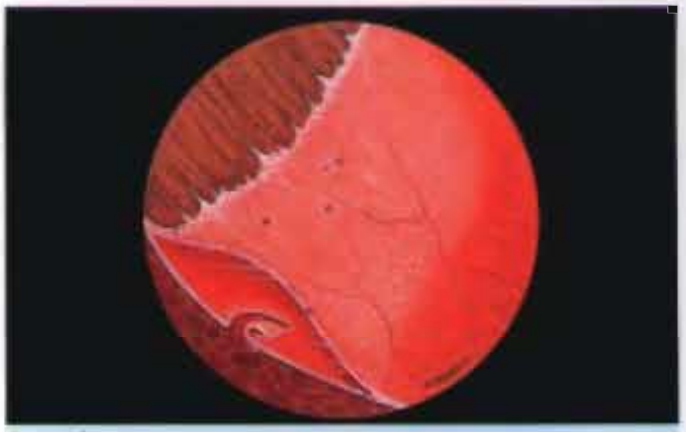

Fig. 12.40
Degenerative retinoschisis with holes in both layers: snowflakes and 'silver-wiring' of blood vessels on the inner layer; the cavity is bridged by torn grey-white tissue

Fig. 12.41
Degenerative retinoschisis with snowflakes and outer layer breaks (Courtesy of N.E Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence California, 1982)

- Breaks may develop in the reticular type. Inner layer breaks are small and round (*see* Fig. 12.40), while the less common outer layer breaks are usually larger, with rolled edges and located behind the equator (Figs 12.41, 12.42a).
- RD is very rare, but may develop in eyes with breaks in both layers. Eyes with only outer layer breaks do not as a rule develop RD because the fluid within the schisis cavity is viscous and does not pass readily into the subretinal space. Rarely, however, the schisis fluid loses its viscosity and passes through the break into the subretinal space, giving rise to a localized detachment of the outer retinal layer which is usually confined to the area of retinoschisis (Fig. 12.42b).
- Vitreous haemorrhage is uncommon.

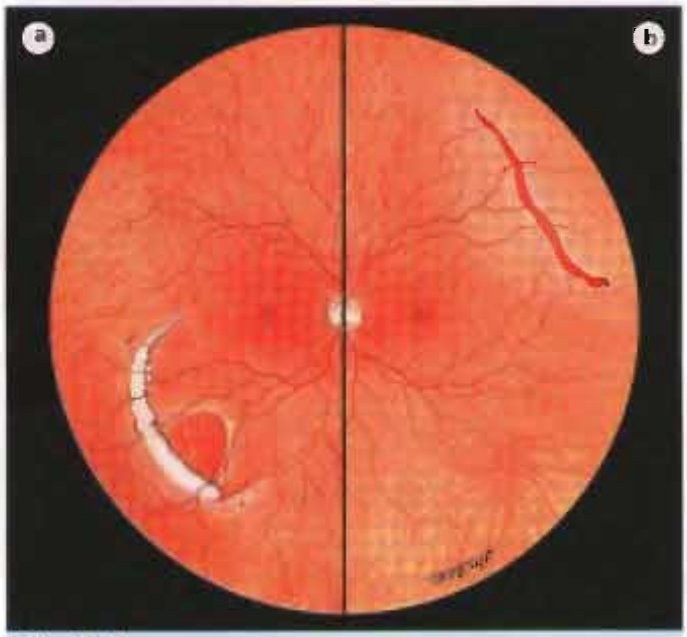

Fig. 12.42
Degenerative retinoschisis. (a) Large breaks in both layers; (b) linear break in the outer layer associated with a localized retinal detachment

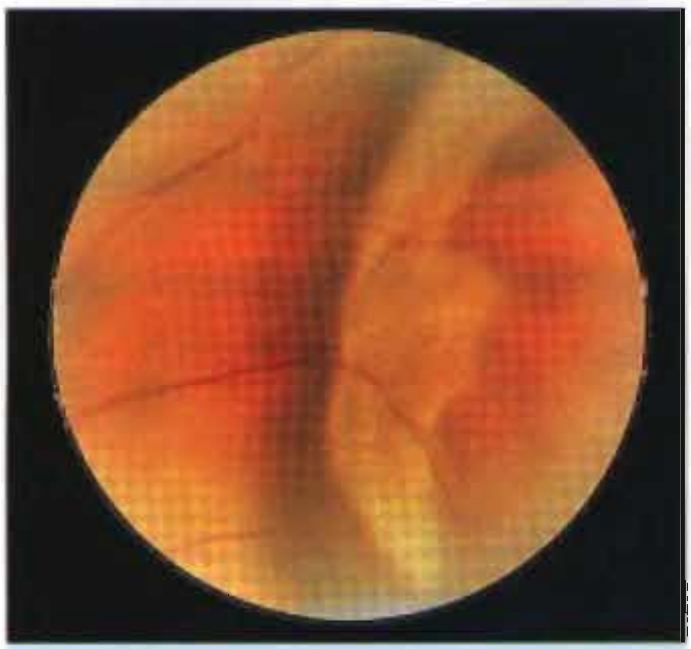

Fig. 12.43
White-with-pressure (Courtesy of N.E. Byer, *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence, California, 1982)

'White-without-pressure'

1. Signs

a. 'White-*with*-pressure' is a translucent grey appearance of the retina, induced by indenting the sclera (Fig. 12.43). Each area has a fixed configuration which does not change when the scleral indentor is moved to an adjacent area. It is often seen in normal eyes and may be observed along the posterior border of islands of lattice degeneration, snailtrack degeneration and outer layer of acquired retinoschisis.

b. 'White-*without*-pressure' has a similar appearance but is present without scleral indentation. On cursory examination a normal area of retina surrounded by

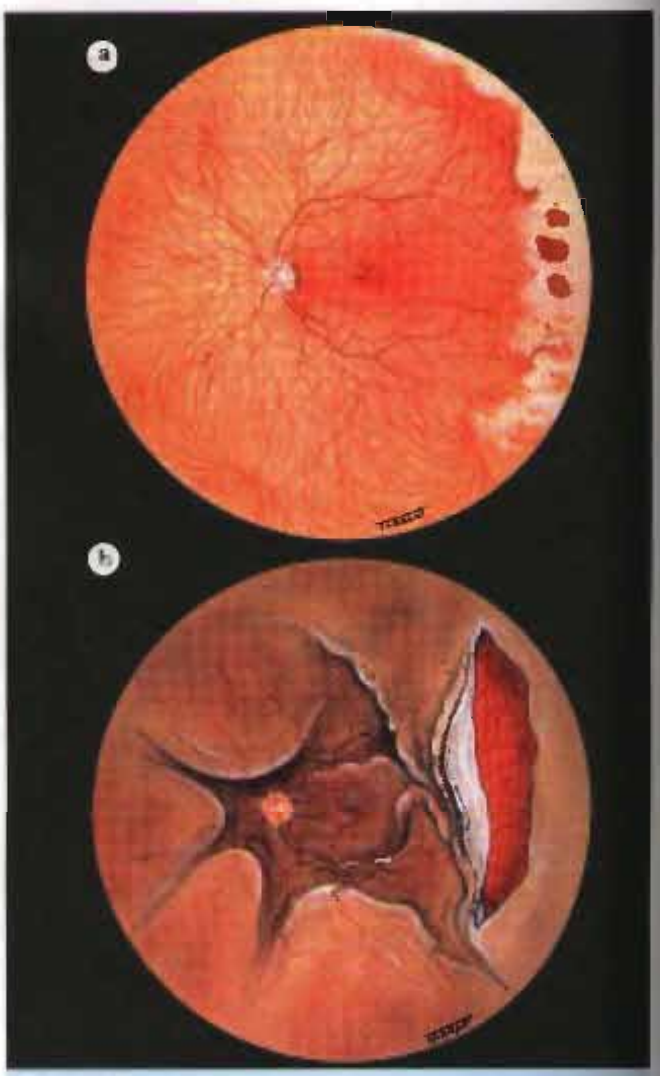

Fig. 12.44
(a) White-without-pressure with pseudo-holes; (b) total retinal detachment due to a giant tear

'white-*without*-pressure' may be mistaken for a flat retinal hole (Fig. 12.44a).

2. **Complications**. Giant tears occasionally develop along the posterior border of an area of 'white-*without*-pressure' (Fig. 12.44b).

Significance of myopia

Although myopes constitute 10% of the general population, over 40% of all RDs occur in myopic eyes. The higher the refractive error the greater the risk of RD. The following interrelated factors predispose the myopic eye to RD:

1. **Lattice degeneration** is more common in moderate myopes and may give rise to tears or holes.
2. **Snailtrack degeneration** is common in myopic eyes and may be associated with holes.
3. **Diffuse chorioretinal atrophy** may give rise to small holes in highly myopic eyes.
4. **Macular holes** may give rise to RD in highly myopic eyes.
5. **Vitreous degeneration** and PVD are more common.
6. **Vitreous loss** during cataract surgery, particularly if inappropriately managed, is associated with about a 15% incidence of subsequent RD in myopic eyes greater than 6 D; the risk is even higher if myopia is more than 10 D.
7. **Posterior capsulotomy** is associated with an increased risk of RD in myopic eyes.

Clinical features of retinal detachment

Rhegmatogenous retinal detachment

Symptoms

The classic premonitory symptoms reported in about 60% of patients with spontaneous rhegmatogenous RD are photopsia and vitreous floaters. After a variable period of time the patient notices a relative peripheral visual field defect which may progress to involve central vision.

1. **Photopsia** in eyes with acute PVD is probably caused by traction on the retina at sites of vitreoretinal adhesion. Cessation of photopsia is the result of either separation of the adhesion or complete tearing away of a piece of retina (operculum) at the site of adhesion. In eyes with PVD the photopsia may be induced by eye movements and is more noticeable in dim illumination. It tends to be projected into the temporal peripheral visual field and, unlike floaters, has no lateralizing value.
2. **Floaters** are moving vitreous opacities perceived when they cast a shadow upon the retina. Vitreous opacities in eyes with acute PVD are of the following three types:
   a. *A **solitary ring-shaped opacity*** representing the detached annular attachment to the margin of the optic disc (Weiss ring) (*see* Fig. 12.20).
   b. ***Cobwebs*** are caused by condensation of collagen fibres within the collapsed vitreous cortex.
   c. *A **sudden shower*** of minute red-coloured or dark spots usually indicates vitreous haemorrhage secondary to tearing of a peripheral retinal blood vessel.
3. **A visual field defect** secondary to RD is perceived as a dark curtain. In some patients it may not be present on waking in the morning due to spontaneous absorption of SRF, only to reappear later in the day. The quadrant of the visual field in which the defect first appears is useful in predicting the location of the primary retinal break (which will be in the opposite quadrant). Loss of central vision may be due either to involvement of the fovea by SRF or, less frequently, obstruction of the visual axis by a large upper bullous RD (Fig. 12.45).

Fig. 12.45
Fresh superior bullous retinal detachment

Fig. 12.46
Tobacco dust and cobweb-like opacities associated with retinal detachment (Courtesy of V. Tanner)

General signs

- A Marcus Gunn pupil (relative afferent pupillary defect) is present in eyes with extensive RDs irrespective of the type.
- The intraocular pressure is usually lower than in the normal eye by about 5 mmHg.
- A mild anterior uveitis is very common.
- The anterior vitreous shows 'tobacco dust' (Fig. 12.46).
- Retinal breaks appear as red discontinuities in the retinal surface (Fig. 12.47).

Fig. 12.47
Retinal tears in detached retina

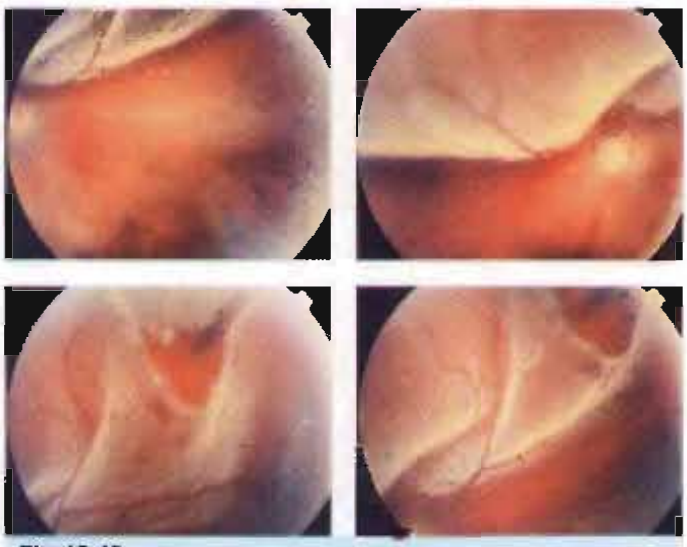

Fig. 12.48
Fresh retinal detachment due to a large U-shaped tear with mobile subretinal fluid (Courtesy of S. Milewski)

- Retinal signs depend on the duration of RD and the presence or absence of proliferative vitreoretinopathy as described below.

Fresh retinal detachment

- The detached retina has a convex configuration and a slightly opaque and corrugated appearance due to intraretinal oedema. It undulates freely with eye movements (Fig. 12.48).
- There is loss of the underlying choroidal pattern and the retinal blood vessels appear darker than in flat retina, so that the colour contrast between venules and arterioles is less apparent.
- The SRF extends up to the ora serrata except in the rare cases caused by a macular hole, in which the SRF is initially confined to the posterior pole.
- A pseudo-hole is frequently seen if the posterior pole is detached.

> ***NB:*** This should not be mistaken for a true macular hole which may give rise to RD in highly myopic eyes or following blunt ocular trauma.

Old retinal detachment

The following are the main features of a long-standing rhegmatogenous RD which do not occur in any other type of RD irrespective of duration (Fig. 12.49).

- Retinal thinning secondary to atrophy, which must not be mistaken for retinoschisis.
- Secondary intraretinal cysts may develop if the RD has been present for over a year (Fig. 12.50).
- Subretinal demarcation lines (high-water marks) caused by proliferation of RPE cells at the junction of flat and

Fig. 12.49
Long-standing inferior retinal detachment associated with a secondary intraretinal cyst and a pigmented demarcation line

Fig. 12.50
Secondary intraretinal cyst (Courtesy of N.E. Byer, from *The Peripheral Retina in Profile, a Stereoscopic Atlas*. Criterion Press, Torrence, California, 1982)

Fig. 12.52
Retinal tears with rolled edges in grade B proliferative vitreoretinopathy

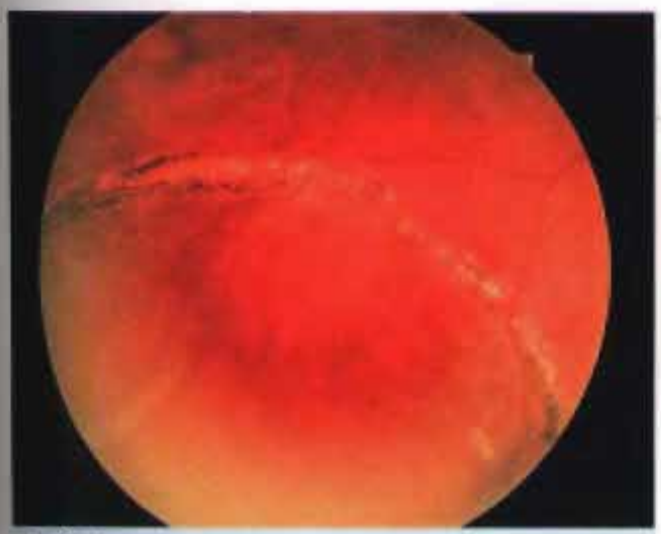

Fig. 12.51
Inferior retinal detachment demarcated by a pigmented line

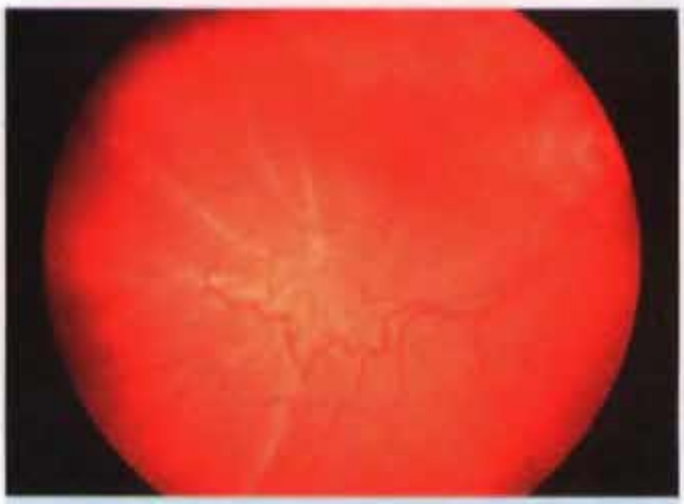

Fig. 12.53
Retinal wrinkling and vascular distortion in grade B proliferative vitreoretinopathy

detached retina are common and take about 3 months to develop (Fig. 12.51).

Proliferative vitreoretinopathy

Proliferative vitreoretinopathy (PVR) is caused by the proliferation and contraction of membranes on the inner retinal surface (epiretinal membranes), on the posterior surface of the detached hyaloid and occasionally also on the outer retinal surface (subretinal membranes). Severe postoperative contraction of these membranes is the most common cause of failure of RD surgery. The main clinical signs of PVR are retinal folds and rigidity so that retinal undulation induced by eye movements or scleral indentation is decreased according to severity. The classification of PVR is as follows:

1. **Grade A** (minimal) is characterized by diffuse vitreous haze, 'tobacco dust' and occasionally pigmented cells on the inferior retina.
2. **Grade B** (moderate) is characterized by retinal breaks with rolled irregular edges (Fig. 12.52), wrinkling of the inner retinal surface and tortuous blood vessels (Fig. 12.53), retinal stiffness and decreased mobility of vitreous gel. The epiretinal membranes responsible for these findings cannot be identified by indirect ophthalmoscopy, although they may be visualized on slit-lamp non-contact indirect ophthalmoscopy.

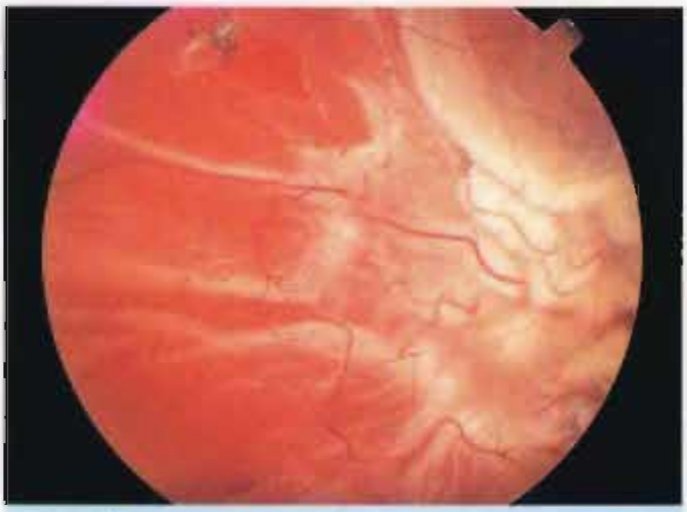

Fig. 12.54
Fixed retina folds in grade C proliferative vitreoretinopathy

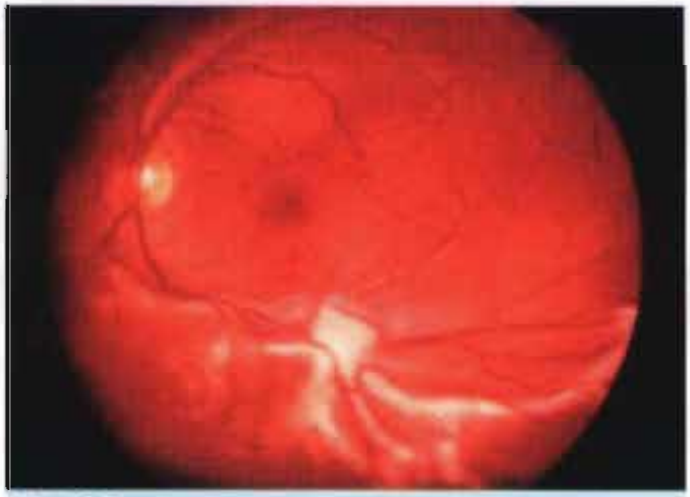

Fig. 12.55
Grade C type 1 (focal) proliferative vitreoretinopathy

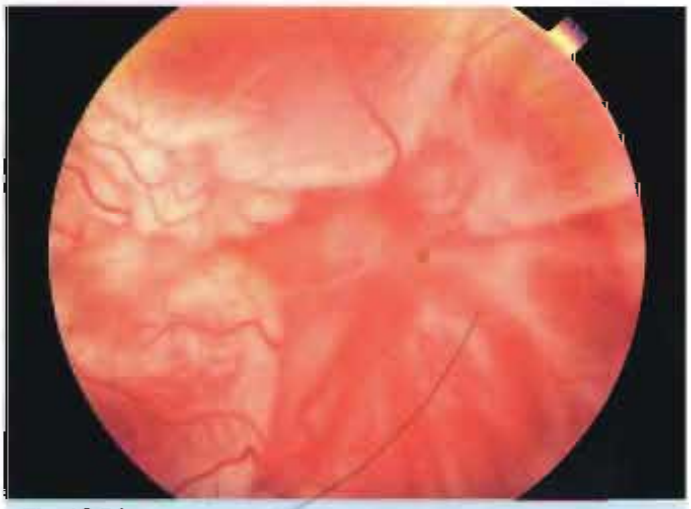

Fig. 12.56
Grade C type 2 (diffuse) proliferative vitreoretinopathy

Fig. 12.57
Grade C type 3 (subretinal) proliferative vitreoretinopathy

3. **Grade C** (severe) is characterized by full-thickness rigid retinal folds (Fig. 12.54) with heavy vitreous condensation and strands. It may be anterior or posterior, the rough dividing line being the equator of the globe.
   a. The severity of proliferation is expressed by the number of clock hours of retina involved (1–12), although proliferations need not be contiguous.
   b. The type of contraction is further subdivided into: type 1 (focal) (Fig. 12.55), type 2 (diffuse) (Fig. 12.56), type 3 (subretinal) (Fig. 12.57), type 4 (circumferential) and type 5 (anterior displacement).

Tractional retinal detachment

1. **Symptoms.** Photopsia and floaters are usually absent because vitreoretinal traction develops insidiously and is not associated with acute PVD. The visual field defect usually progresses slowly and may become stationary for months or even years.
2. **Signs**
   - The detached retina is concave and breaks are absent (Fig. 12.58).
   - The SRF is shallower than in a rhegmatogenous RD and seldom extends to the ora serrata (Fig. 12.59).
   - The highest elevation of the retina occurs at sites of vitreoretinal traction.
   - Retinal mobility is severely reduced and shifting fluid is absent.

NB: If a tractional RD develops a break it assumes the characteristics of a rhegmatogenous RD and progresses more quickly (combined tractional–rhegmatogenous RD) (Fig. 12.60).

Fig. 12.58
Inferior tractional retinal detachment in proliferative diabetic retinopathy

Fig. 12.60
Combined tractional–rhegmatogenous retinal detachment in proliferative diabetic retinopathy

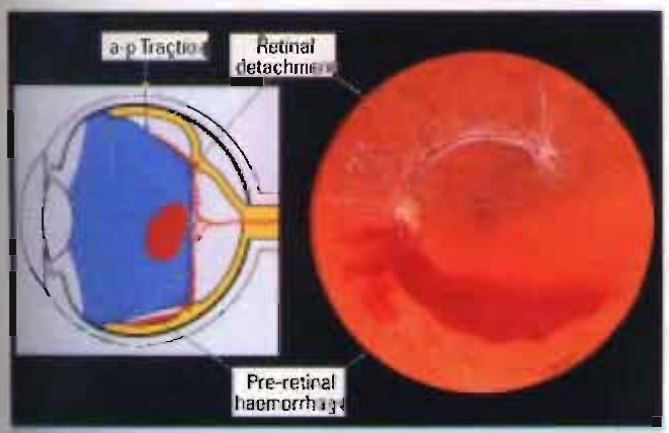

Fig. 12.59
Superior tractional retinal detachment in proliferative diabetic retinopathy

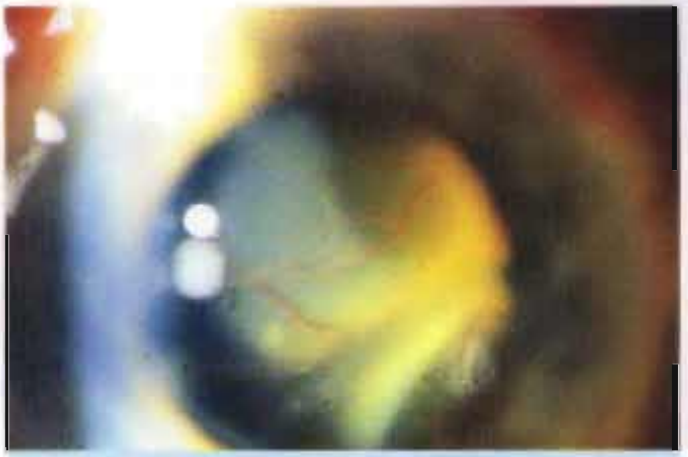

Fig. 12.61
Exudative retinal detachment

Exudative retinal detachment

1. **Symptoms.** Photopsiae are absent because there is no vitreoretinal traction although floaters may be present if there is associated vitritis. The visual field defect may develop suddenly and progress rapidly. In some cases of Harada disease both eyes may be involved simultaneously.
2. **Signs**
   - The detached retina is convex and retinal breaks are absent.
   - The surface is smooth rather than corrugated.
   - Occasionally the SRF is so deep that the RD may be seen on the slit-lamp without the aid of a lens (Fig. 12.61); the retina may even touch the back of the crystalline lens.
   - The detached retina is very mobile and exhibits the phenomenon of 'shifting fluid' in which SRF responds to the force of gravity and detaches the area of retina under which it accumulates. For example, in the upright position the SRF collects under the inferior retina but on assuming the supine position the inferior retina flattens and the SRF shifts posteriorly, detaching the macula and superior retina.
   - Scattered areas of subretinal clumping giving rise to characteristic 'leopard spots' may be seen after the detachment has resolved (Fig. 12.62).
   - The cause of the RD, such as a choroidal tumour (Fig. 12.63), may be apparent when the fundus is examined.

Fig. 12.62
'Leopard spot' pigmentation following resolution of exudative retinal detachment

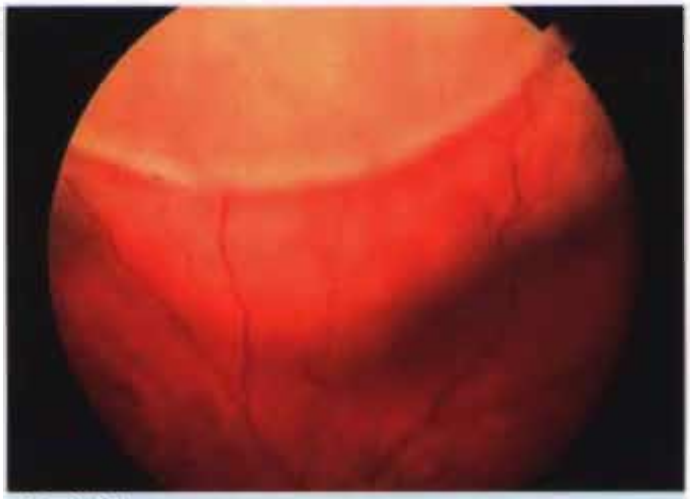

Fig. 12.63
Choroidal metastasis with overlying exudative retinal detachment (Courtesy of J. Shields and A. Singh)

Differential diagnosis of retinal detachment

Degenerative retinoschisis

1. **Symptoms.** Photopsia and floaters are absent because there is no vitreoretinal traction. A visual field defect is seldom observed because posterior spread is rare. If present it is absolute.
2. **Signs** (see Figs 12.38, 12.39 and 12.40)
   - The elevation is convex, smooth, thin and immobile.
   - The thin inner leaf of the schisis may be mistaken, on cursory examination, for an atrophic long-standing rhegmatogenous RD. However, demarcation lines and secondary cysts in the inner leaf are absent in retinoschisis.
   - Breaks may be present in one or both layers in eyes with reticular retinoschisis.

Choroidal detachment

1. **Symptoms.** Photopsia and floaters are absent because there is no vitreoretinal traction. A visual field defect may be present in an eye with a large choroidal detachment.
2. **Signs**
   - The intraocular pressure may be very low as a result of concomitant detachment of the ciliary body.
   - A choroidal detachment is a brown, convex, smooth, bullous elevation, which is relatively immobile (Fig. 12.64).
   - The peripheral retina and ora serrata may be seen without scleral indentation (Fig. 12.65).

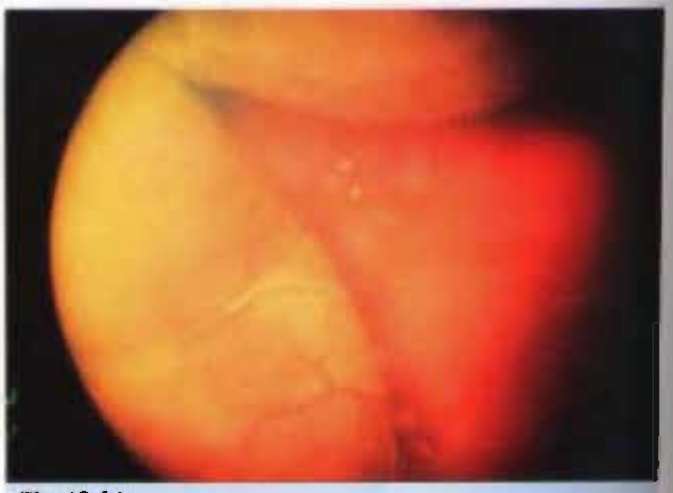

Fig. 12.64
Choroidal detachment

Fig. 12.65
Choroidal detachment with visibility of the pars plana (Courtesy of P. Morse)

- The elevations do not extend to the posterior pole because they are limited by the firm adhesion between the suprachoroidal lamellae and the sclera where the vortex veins enter their scleral canals.

Uveal effusion syndrome

The uveal effusion syndrome is a rare, idiopathic condition characterized by choroidal detachments associated with exudative RD (Fig. 12.66). Following resolution, the RPE frequently shows a characteristic residual mottling.

NB: Uveal effusion may be mistaken for either RD complicated by choroidal detachment or ring melanoma of the anterior uvea.

Fig. 12.66
Uveal effusion syndrome characterized by choroidal detachment and exudative retinal detachment

Prophylaxis of rhegmatogenous retinal detachment

Retinal breaks

Although, given the right circumstances, any retinal break may cause an RD, some are more dangerous than others. Important criteria in the selection of patients for prophylactic treatment can be divided into (a) *type of break* and (b) *other considerations*.

Type of break

1. **Tears** are more dangerous than holes because they are associated with dynamic vitreoretinal traction.
2. **Large breaks** are more dangerous than small ones because of increased access to the subretinal space.
3. **Symptomatic breaks** are more dangerous than those detected by chance because they are associated with dynamic vitreoretinal traction.
4. **Superior breaks** are more dangerous than inferior breaks because SRF is likely to spread more quickly.
5. **Equatorial breaks** are more dangerous than oral breaks, which seldom give rise to RD.
6. **A subclinical RD** constitutes a break surrounded by a very small amount of SRF. In some cases the SRF may spread and the RD become 'clinical' within a short period of time.
7. **Pigmentation** around a retinal break indicates that it is long-standing with a small risk of RD.

Other considerations

1. **Aphakic** patients are at increased risk of RD, particularly when surgery has been complicated by vitreous loss. Even relatively innocuous small peripheral round holes may on occasion give rise to RD following cataract surgery.
2. **Myopic** patients are more prone to RD. A break in a myopic eye should be taken more seriously than a similar lesion in a non-myopic eye.
3. **One-eyed** patients with breaks should be taken seriously, particularly if the fellow eye has lost vision from RD.
4. **Family history** may occasionally be relevant; any break or predisposing degeneration should be taken seriously if the patient has a positive family history of RD.
5. **Systemic diseases** associated with an increased risk of RD include Marfan syndrome, Stickler syndrome and Ehlers–Danlos syndrome. Because RD in these patients has a relatively poor prognosis, any break or predisposing degeneration should be treated prophylactically.

Clinical examples (Fig. 12.67a–h)

a. A large equatorial U-tear associated with subclinical RD located in the upper temporal quadrant should be treated prophylactically without delay because the risk of progression to a clinical RD is high. As the tear is located in the upper temporal quadrant, early macular involvement by SRF is likely.

b. A large U-tear in the upper temporal quadrant in an eye with symptomatic, acute PVD should also be treated without delay because the risk of progression to clinical RD is high.

c. An operculated tear bridged by a patent blood vessel should be treated because persistent dynamic vitreoretinal traction on the bridging blood vessel may cause recurrent vitreous haemorrhage.

d. A tear with a free-floating operculum in the lower temporal quadrant detected by chance is much safer because there is no vitreoretinal traction. Prophylaxis is therefore not required in the absence of other risk factors.

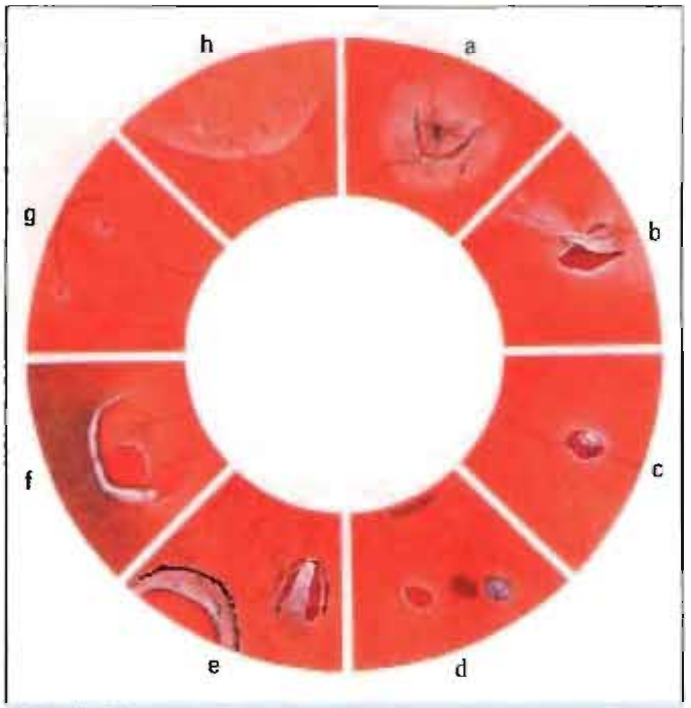

Fig. 12.67
Prophylactic treatment of retinal breaks (see *text*)

e. An inferior U-tear and a dialysis surrounded by pigment detected by chance are both long-standing very low-risk lesions.
f. Degenerative retinoschisis, even with breaks in both layers, does not require treatment. Although this lesion represents a full-thickness defect in the sensory retina, the fluid within the schisis cavity is usually viscid and rarely passes into the subretinal space.
g. Two small asymptomatic holes near the ora serrata do not require treatment: the risk of RD is extremely small as they are probably located within the vitreous base. About 5% of the general population have such lesions.
h. Small inner layer holes in retinoschisis also carry an extremely low risk of RD as there is no communication between the vitreous cavity and the subretinal space.

Predisposing peripheral retinal degenerations

In the absence of associated retinal breaks neither lattice nor snailtrack degenerations merit prophylactic treatment unless associated with one or more of the following risk factors:

1. **RD in the fellow eye** is the most frequent indication.
2. **Aphakia or pseudophakia**, particularly if laser posterior capsulotomy is necessary.
3. **High myopia**, particularly if associated with extensive lattice degeneration.
4. **Strong family history of RD.**
5. **Systemic disease** known to predispose to RD, such as Marfan syndrome, Stickler syndrome and Ehlers–Danlos syndrome.

Treatment modalities

Choice of modality

Prophylactic treatment modalities are (a) *cryotherapy*, (b) *slit-lamp laser photocoagulation* and (c) *indirect ophthalmoscopic laser photocoagulation* combined with scleral indentation. In most cases the choice is based on personal preference and experience as well as the availability of instrumentation. Other considerations include:

1. **Location of lesion**
   - An equatorial lesion can be treated by either photocoagulation or cryotherapy.
   - A post-equatorial lesion can be treated only by photocoagulation unless the conjunctiva is incised.
   - Lesions near the ora serrata can be treated either by cryotherapy or laser photocoagulation using the indirect ophthalmoscope delivery system combined with indentation. Laser photocoagulation using a slit-lamp delivery system is difficult in these cases and it may be impossible to adequately treat the base of a U-tear.
2. **Clarity of media.** Eyes with hazy media are much easier to treat by cryotherapy.
3. **Pupil size.** Eyes with small pupils are easier to treat by cryotherapy.

Slit-lamp laser photocoagulation

1. **Technique**
   a. Laser settings are 200 μm spot size and duration of 0.1–0.2 seconds.
   b. A triple-mirror or a wide field (panfundoscopic) lens is inserted under topical anaesthesia.
   c. The lesion is surrounded by two rows of confluent burns of moderate intensity (Figs 12.68, 12.69).
   d. After treatment the patient is advised to avoid strenuous physical exertion for about 7 days until an adequate adhesion has formed and the lesion is securely sealed.

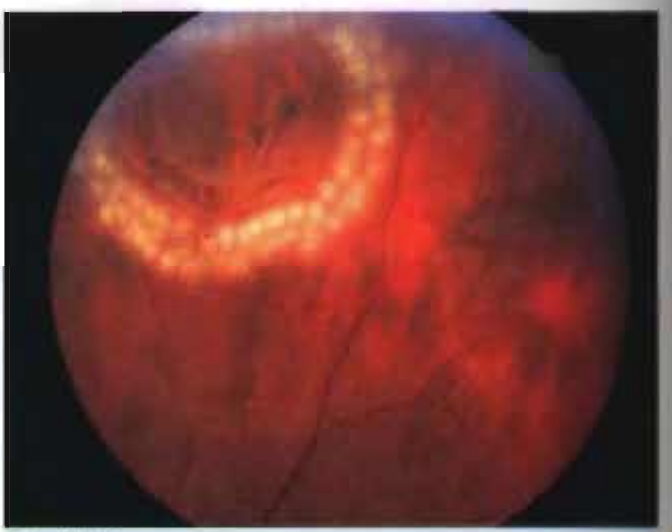

Fig. 12.68
Appearance soon after prophylactic laser photocoagulation of a retinal break

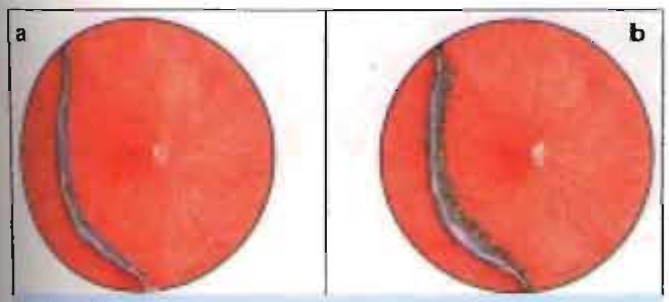

Fig. 12.69
(a) Large traumatic retinal dialysis; (b) several weeks after prophylactic laser photocoagulation

2. **Potential problems.** Serious complications from peripheral retinal photocoagulation are uncommon and usually associated with excessively heavy treatment to large areas of the retina.
   - Maculopathy in the form of cystoid macular oedema or macular pucker (*see* Fig. 12.101).
   - Choroidal detachment, which may be complicated by secondary angle-closure glaucoma as a result of a forward rotation of the ciliary body.
   - Exudative RD, which usually resolves within 1 or 2 weeks.
   - Rhegmatogenous RD caused by secondary tear formation is very rare.
   - Retinal haemorrhage is rare and can usually be stopped by pressing the contact lens against the eye in order to increase intraocular pressure.

Cryotherapy

1. **Technique**
   a. The eye is anaesthetized with a pledget soaked in amethocaine or a subconjunctival injection of lignocaine in the quadrant of the lesion.
   b. For post-equatorial lesions, a small conjunctival incision may be necessary to enable the cryoprobe to reach the required location.
   c. While viewing with the indirect ophthalmoscope, the sclera is gently indented with the tip of the probe.
   d. The lesion is surrounded with a single row of cryoapplications; freezing is terminated as soon as the retina whitens.
   e. The cryoprobe should not be removed until it has defrosted completely because premature removal may 'crack' the choroid and give rise to a choroidal haemorrhage.
   f. The eye is padded for about 4 hours to prevent chemosis and the patient advised to refrain from strenuous physical activity for a week.

   For about 2 days the treated area appears whitish due to oedema. After about 5 days pigmentation begins to appear. Initially the pigment is fine; later it becomes coarser and is associated with a variable amount of chorioretinal atrophy (Fig. 12.70).

2. **Potential problems**
   - Chemosis and lid oedema are common and innocuous.
   - Transient diplopia may occur as a result of freezing of an extraocular muscle.

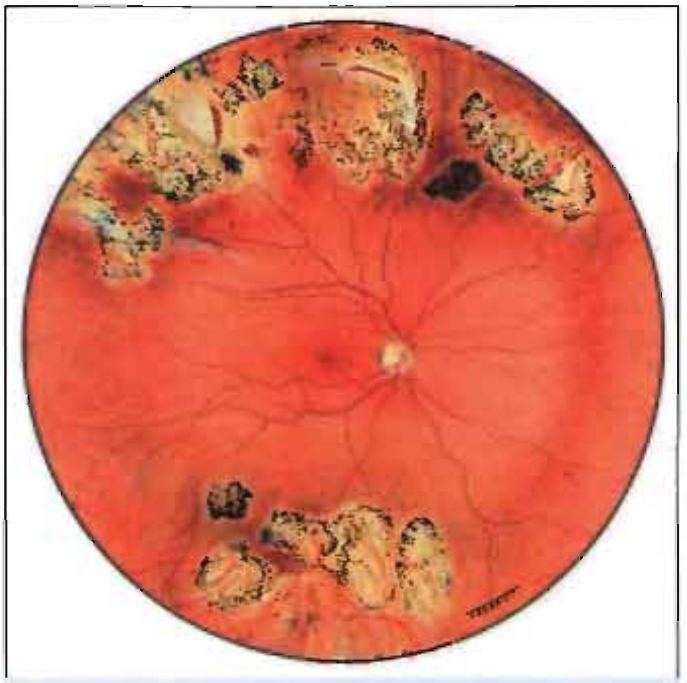

Fig. 12.70
Pigmentation and chorioretinal atrophy following prophylactic cryotherapy

   - Vitritis may occur as a result of excessively heavy treatment.
   - Maculopathy is rare.

Causes of failure

The two main causes of failure of prophylaxis are (a) *inadequate treatment* and (b) *new break formation.*

1. **Inadequate treatment** may be due to the following:
   - Failure to surround the lesion with two rows of burns, particularly the base of a U-tear, is the most common cause of failure. If the most peripheral part of the tear

Fig. 12.71
New breaks at 7 and 12 o'clock with subretinal fluid following extensive cryotherapy of lattice degeneration

cannot be reached by photocoagulation then cryotherapy should be employed.
- Failure to apply contiguous treatment when treating a large break or a dialysis.
- Failure to release dynamic vitreoretinal traction on a large U-tear by inserting an explant and failure to use an explant in an eye with a subclinical RD (*see* below).

2. **New break formation** may occur in the following two sites:
   - Within or adjacent to the treated area, usually caused by excessively heavy treatment, particularly of lattice degeneration (Fig. 12.71).
   - In 'normal' appearing retina despite adequate treatment of the predisposing lesion. This is one of the limitations of prophylactic treatment.

Lesions not requiring prophylaxis

It is important to recognize the following entirely innocuous peripheral retinal degenerations which do not require prophylaxis (Fig. 12.72a–f):

a. **Microcystoid degeneration** consists of tiny vesicles with indistinct boundaries on a greyish-white background which make the retina appear thickened and less transparent (*see* Fig. 12.5).
b. **Snowflakes** are minute glistening yellow-white dots which are frequently found scattered diffusely in the peripheral fundus. Foci composed solely of snowflakes are innocuous and require no treatment.

NB: Snowflakes are, however, of considerable clinical importance because, as mentioned previously, they are frequently associated with lattice degeneration, snailtrack degeneration and acquired retinoschisis.

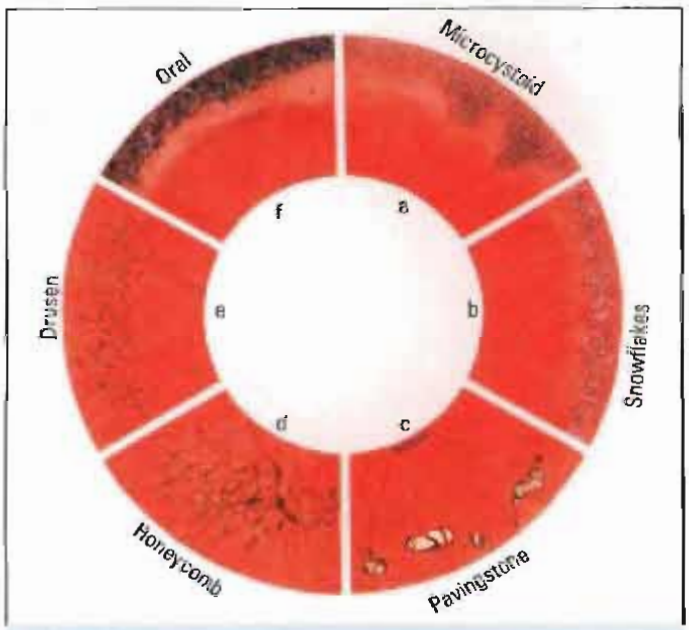

Fig. 12.72
Benign peripheral retinal degenerations

Fig. 12.73
Pavingstone degeneration

Fig. 12.74
Honeycomb degeneration

Fig. 12.75
Peripheral drusen

c. **Pavingstone degeneration** is characterized by discrete yellow-white patches of focal chorioretinal atrophy, present to some extent in 25% of normal eyes (Fig. 12.73).
d. **Honeycomb (reticular) degeneration** is an age-related change characterized by a fine network of perivascular pigmentation which may extend posterior to the equator (Fig. 12.74).
e. **Drusen** (colloid bodies) are clusters of small pale lesions which may have hyperpigmented borders (Fig. 12.75).
f. **Oral pigmentary degeneration** is an age-related change consisting of a hyperpigmented band running adjacent to the ora serrata.

Standard retinal surgery

Prognosis for central vision

The main factor governing eventual visual function, provided the retina has been successfully reattached, is the duration of macular involvement by the RD.

- Most eyes with macula-on RD maintain their preoperative visual acuity.
- Within the first week after development of macula-off RD, delay in surgery does not adversely affect visual outcome.
- Macula-off RD of less than 2 months duration results in some impairment of visual acuity but there is no direct correlation between the duration of macular detachment and final visual acuity.
- Macula-off RD of over 2 months duration results in poor visual acuity which appears to be related to the duration of macular involvement.

Principles of scleral buckling

Scleral buckling involves the creation of inward indentation of the sclera ('buckle'). The two main purposes are: (a) *to close retinal breaks* by apposing the RPE to the sensory retina and (b) *to reduce dynamic vitreoretinal traction* at sites of local vitreoretinal adhesion. An explant is material sutured directly onto the sclera to create a buckle.

Local explants

1. **Configuration**
   a. *Radial* explants are placed at right angles to the limbus (Fig. 12.76a).
   b. *Circumferential* explants are placed parallel to the limbus to create a segmental buckle (Fig. 12.76b).
2. **Dimensions.** In order to adequately seal a retinal break it is essential that the buckle be positioned accurately and is of adequate length, width and height.
   a. ***The width*** of a *radial buckle* depends on the width (distance between anterior horns) of the retinal tear and its length depends on the length (distance between base and apex) of the tear. In general, the dimensions of the explant should be twice that of the tear. The required width and length of a *segmental circumferential buckle* depend on the length and width, respectively, of the tear.
   b. ***The height*** is determined by the following interrelated factors:
      - The greater the diameter of the explant, the higher the buckle.
      - The greater the separation of sutures, the higher the buckle.
      - The tighter the sutures over the explant, the higher the buckle.
      - The lower the intraocular pressure, the higher the buckle.
3. **Indications for radial buckling**
   - Large U-tears because there is less tendency to 'fishmouth' (*see* below).
   - Relatively posterior breaks because sutures are easier to insert.
4. **Indications for segmental circumferential buckling**
   - Multiple breaks located in one or two quadrants.
   - Anterior breaks because they can be closed more easily.
   - Wide breaks such as dialyses.

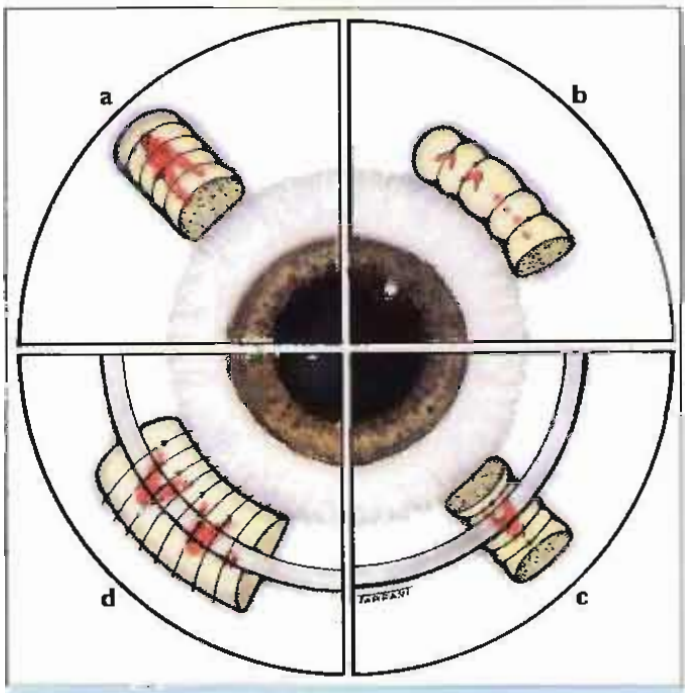

Fig. 12.76
Configuration of scleral buckles. (a) Radial sponge; (b) circumferential sponge; (c) encirclement augmented by a radial sponge; (d) encirclement augmented by a solid silicone tyre

Encircling explants

Encircling explants are placed around the entire circumference of the globe to create a 360° buckle (Fig. 12.76c and d).

1. **Dimensions.** Straps with a diameter of 2 mm (no. 40) are most frequently used. A strap induces a fairly narrow buckle, and therefore often has to be supplemented with either radial sponges or circumferential solid silicone tyres to support large tears. A 2 mm high buckle may be produced by tightening the strap by about 12 mm. In contrast to a local explant, the buckle produced by a strap is permanent.
2. **Indications**
   - Breaks involving three or more quadrants.
   - Lattice or snailtrack degeneration involving three or more quadrants.
   - Extensive RD without detectable breaks, particularly in eyes with hazy media.
   - Failed local procedures in which the reason for failure is not apparent.

Drainage of subretinal fluid

Drainage of SRF affords immediate apposition between the sensory retina and RPE. Although a large proportion of RDs can be treated successfully with non-drainage techniques, drainage may be required under certain circumstances. This measure is however, not without potential complications (*see* below). Although non-drainage avoids most of these complications it often does not accomplish immediate apposition between the sensory retina and RPE with flattening of the fovea. If such apposition is delayed for more than 5 days, a satisfactory adhesion will not develop around the retinal break because the 'stickiness' of the RPE will have worn off. This may result in non-attachment of the retina or, in some cases, reopening of the break during the postoperative period. In addition, drainage of SRF allows the use of a large bubble of an internal tamponading agent (air or gas).

Scleral buckling techniques

Preliminary steps

1. With spring-scissors, conjunctiva and Tenon capsule are undermined and cut circumferentially at the limbus in the quadrant(s) corresponding to the retinal breaks.
2. A squint hook is inserted under the corresponding rectus muscles (Fig. 12.77) and bridle sutures are placed.
3. The sclera is inspected to detect thinning (Fig. 12.78) or anomalous vortex veins which may influence subsequent suture placement and drainage of SRF.
4. A 5/0 Dacron partial-thickness scleral suture is inserted at the site calculated to correspond to the apex of the tear.
5. The cut suture is grasped with curved mosquito forceps as close to the knot as possible (Fig. 12.79).
6. While viewing with the indirect ophthalmoscope, the sclera is indented by rotating the forceps. If the indentation does not coincide with the break, the procedure is repeated until accurate localization is achieved.
7. The sclera is gently indented with the tip of the cryoprobe (Fig. 12.80) and freezing is activated until the break is surrounded by a 2 mm margin of whitening.

Insertion of local explant

1. An appropriate-sized explant is selected according to the aforementioned criteria.
2. With calipers, the required distance separating the suture bites is measured and marked on the sclera with cautery.

Fig. 12.78
Severe scleral thinning

Fig. 12.77
Insertion of squint hook under a rectus muscle

Fig. 12.79
Localizing suture grasped with mosquito forceps

Fig. 12.80
Cryotherapy

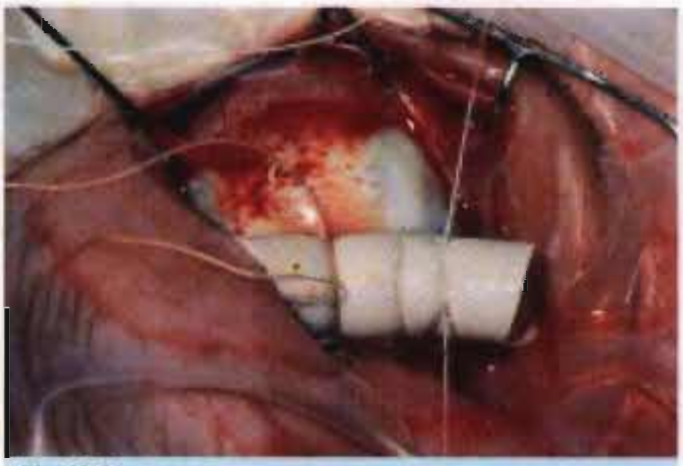

Fig. 12.83
Tying of sutures over sponge

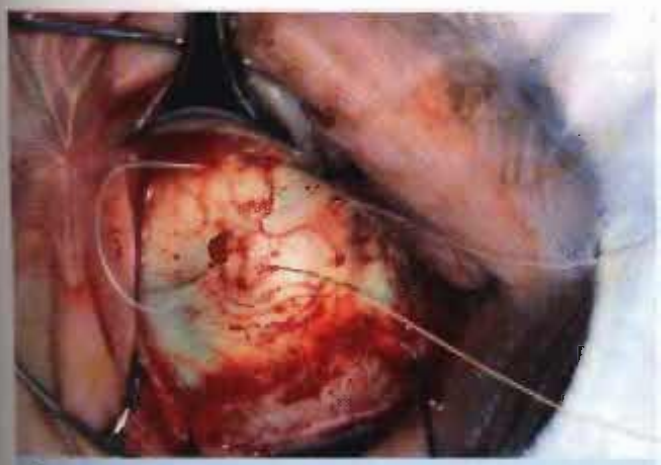

Fig. 12.81
Mattress suture in place

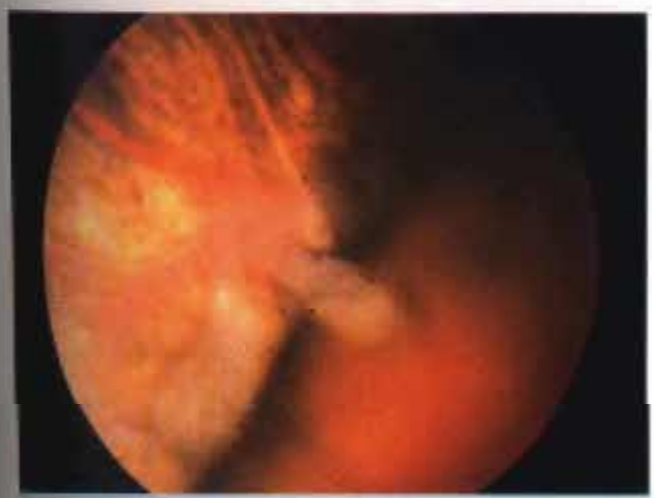

Fig. 12.82
Indentation in relation to the tear—in this case the indentation is too anterior

NB: As a general rule, the separation of sutures should be about one and a half times the diameter of the explant.

3. A mattress-type suture is inserted which will straddle the explant (Fig. 12.81).
4. SRF is drained, if appropriate (*see* below).
5. The position of the break in relation to the buckle is checked (Fig. 12.82) and the buckle is repositioned if necessary.
6. The sutures are tightened over the explant (Fig. 12.83).

Drain-Air-Cryo-Explant (D-A-C-E)

Localization of relatively anterior breaks in eyes with shallow SRF is easy. However, accurate localization may be difficult or impossible in eyes with bullous RDs, especially if the breaks are post-equatorial. The D-A-C-E technique is useful under these circumstances:

1. SRF is drained to bring retina (and thus the break) closer to the RPE.
2. Air is injected into the vitreous cavity to counteract the hypotony induced by drainage.
3. Breaks may then be accurately localized and treated with cryotherapy.
4. The explant is inserted.

Encircling procedure

1. A strap of appropriate diameter is selected.
2. One end of the strap is grasped with curved mosquito forceps and fed under the four recti (Fig. 12.84).
3. The two ends are secured with a Watzke sleeve in the quadrant of commencement (Fig. 12.85).
4. The strap is tightened by pulling on the two ends (Fig. 12.86) until it fits snugly around the ora serrata.
5. The strap is slid posteriorly (about 4 mm) and secured in each quadrant with a holding suture (Fig. 12.87).
6. SRF is drained.
7. The strap is tightened further to produce the required degree of indentation as observed with indirect ophthalmoscopy.

NB: An ideal height is about 2 mm. This is achieved by shortening the circumference of the strap by about 12 mm (Fig. 12.88).

Fig. 12.84
Sliding of end of strap under a rectus muscle

Fig. 12.85
End of strap inserted into Watzke sleeve

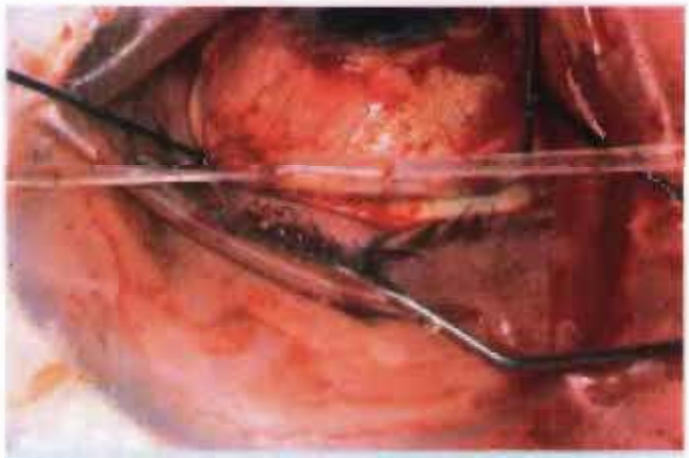

Fig. 12.86
Tightening of strap with Watzke sleeve in position

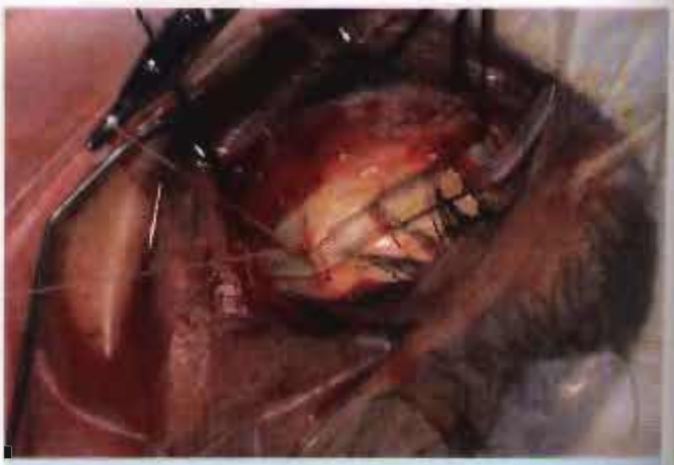

Fig. 12.87
Holding suture in place

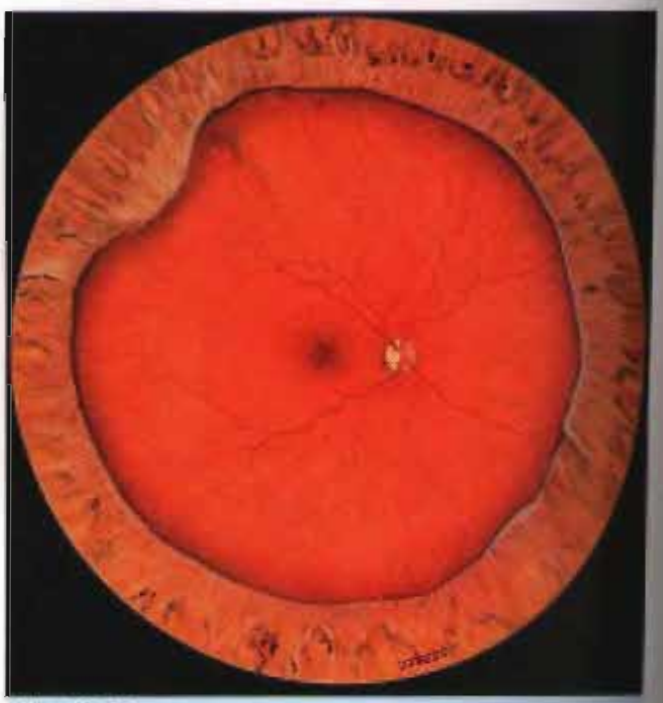

Fig. 12.88
Indentation following encirclement

8. A circumferential buckle should be created such that the retinal breaks 'sit' on the anterior slope of the indentation (the buckle should be placed just behind the breaks).
9. If appropriate, a radial sponge to support a large break (*see* Fig. 12.76c), or a circumferential tyre to support several breaks (*see* Fig. 12.76d) may be inserted under the strap, ensuring that the buckle involves the vitreous base anteriorly.

Drainage of SRF

1. Indications

- Difficulty in localization of breaks in bullous detachments, particularly if the breaks are post-equatorial.
- Immobile retina (e.g. PVR) because a non-drainage procedure will be successful only if the detached retina is sufficiently mobile to move back against the buckle during the postoperative period.
- Long-standing RD because the SRF is viscid and may take months to absorb. Drainage may therefore be necessary, even if the break can be closed without it.
- Inferior RD associated with equatorial tears should ideally be drained because, when the patient assumes the upright position postoperatively, any residual SRF will gravitate inferiorly and may reopen the break.

2. Techniques of drainage have not been standardized. The two most popular methods are described:

a. Method A

- External pressure on the globe is minimized by relaxing traction sutures and lifting the speculum.
- A radial 4 mm sclerotomy is performed, ideally over the area of deepest SRF, and a knuckle of choroid is prolapsed.
- The choroidal knuckle is perforated tangentially with a 25-gauge hypodermic needle on a syringe or a suture needle held by a needle holder (Fig. 12.89).

b. Method B

- The perforation is made directly through sclera, choroid and RPE with the tip of a 27-gauge hypodermic needle bent 2 mm at the tip in a single, swift but controlled fashion.
- In order to prevent haemorrhage from the drainage site, external digital pressure is applied to the globe until the central retinal artery is occluded and complete blanching of the choroidal vascular bed is achieved.
- Pressure is maintained for 5 minutes and the fundus is re-examined; if bleeding is persistent, pressure is reapplied for a further 2 minutes.

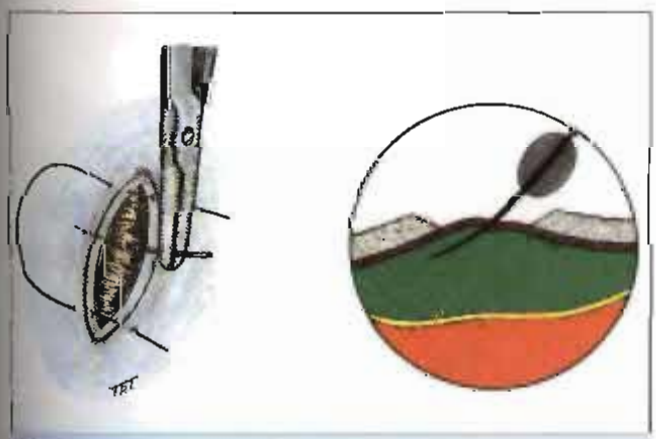

Fig. 12.89
Drainage of subretinal fluid

Fig. 12.90
Subretinal haemorrhage associated with drainage of subretinal fluid

3. Complications

- Haemorrhage (Fig. 12.90), usually due to perforation of a large choroidal vessel.
- Dry tap, in which failure of drainage may be due to incarceration of intraocular structures in the ostium.
- Iatrogenic break formation caused by perforating the retina during drainage.
- Retinal incarceration (Fig. 12.91) is a serious problem, which frequently leads to failure to reattach the retina.
- 'Fishmouthing' is a tendency for U-tears to paradoxically open widely following scleral buckling and drainage of SRF. A tear may communicate with a radial retinal fold rendering it difficult to close (Fig. 12.92a). Management of this problem involves the insertion of

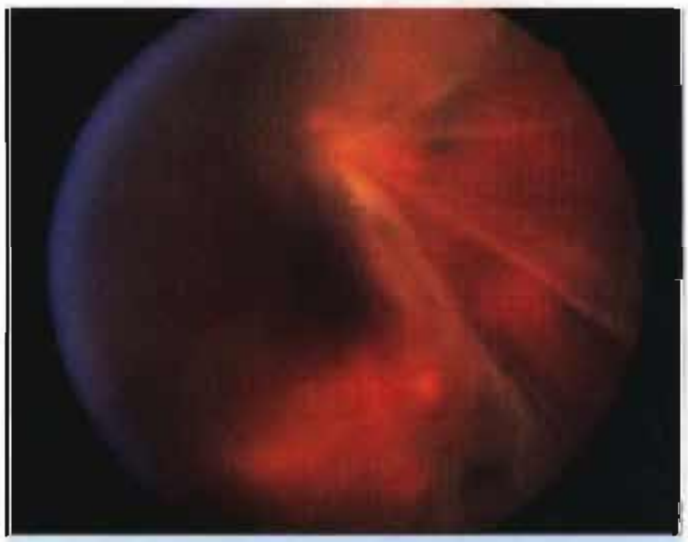

Fig. 12.91
Retinal incarceration into the drainage site

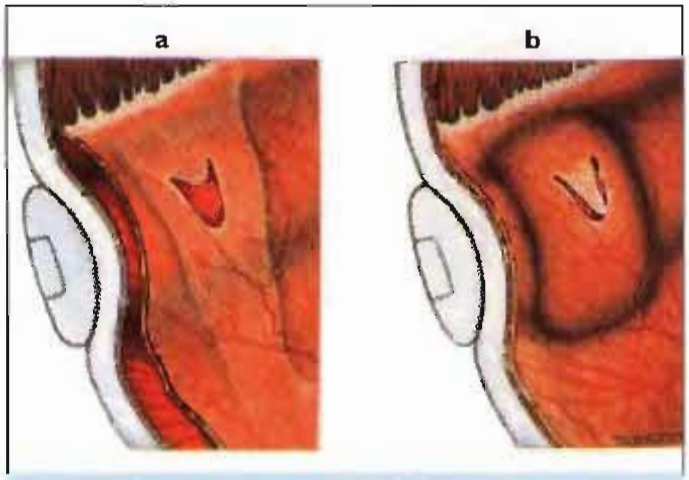

Fig. 12.92
(a) 'Fishmouthing' of a U-tear communicating with a radial fold; (b) insertion of radial buckle

an additional radial buckle and injection of air into the vitreous cavity (Fig. 12.92b).

Intravitreal air injection

1. **Indications**
   - Severe ocular hypotony after drainage of SRF.
   - 'Fishmouthing' of a U-shaped tear.
   - Radial retinal folds.
2. **Technique**
   a. A 25-gauge needle on a 5 ml syringe filled with filtered air is employed.
   b. The globe is steadied and the needle inserted 3.5 mm behind the limbus, through the pars plana.
   c. While viewing through the pupil using the indirect ophthalmoscope without a condensing lens, the needle is aimed at the centre of the vitreous cavity and pushed forward until it is just visible in the pupil.
   d. A single smooth injection is made (Fig. 12.93a).
3. **Potential problems**
   - Loss of visualization of the fundus due to the formation of small air bubbles which may occur if the needle is inserted too deeply into the vitreous cavity (Fig. 12.93b).
   - Elevation of intraocular pressure by injecting too much.
   - Lens damage by the needle, if angled anteriorly.
   - Retinal damage may occur if the needle is inserted too posteriorly.

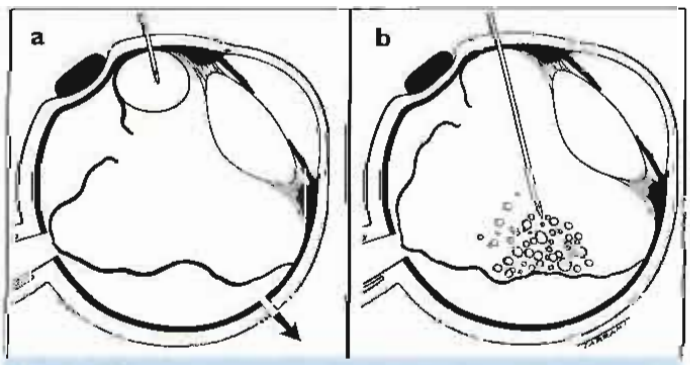

Fig. 12.93
Intravitreal air injection. (a) Correct method; (b) incorrect method

Clinical examples

The following examples emphasize the most important aspects of scleral buckling.

Fresh retinal detachment

1. **Preoperative considerations.** Examination shows a localized right upper temporal RD due to a U-tear (Fig. 12.94a). The prognosis for central vision is good because the macula is uninvolved. The patient should be admitted immediately, rested supine and operated on as soon as possible because the macula is in great danger for two reasons:
   - The break is located in the upper temporal quadrant.
   - Subretinal fluid will spread quickly because the break is large.
2. **Surgical technique**
   a. The peritomy should extend from 8.30 to 12.30 o'clock to expose the lateral and superior recti.
   b. Most U-tears can be sealed with a 5 mm sponge explant. The suture bites should be about 8 mm apart to obtain adequate height to the buckle. The buckle should be placed radially to prevent the possibility of 'fishmouthing' (Fig. 12.94b). Figure 12.94c illustrates an undersized buckle. Accurate positioning of the explant is vital in this case. Figure 12.94d shows a malpositioned buckle.

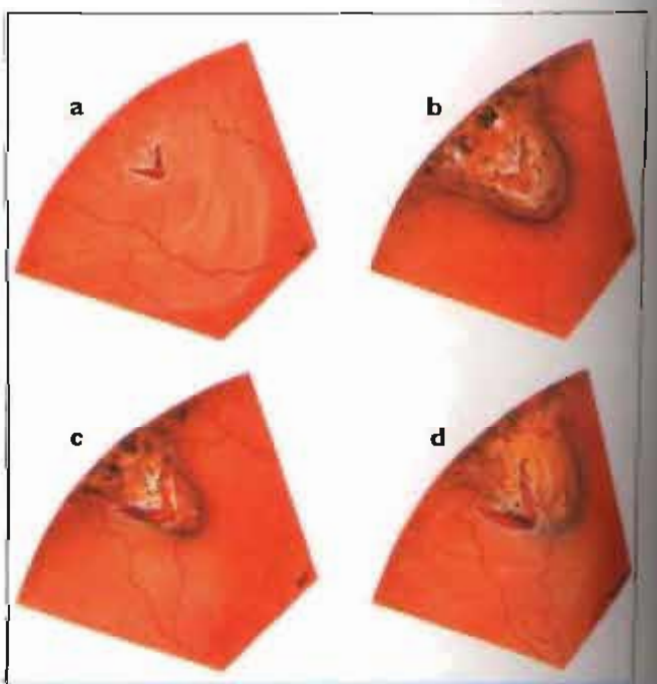

Fig. 12.94
Management of fresh upper temporal retinal detachment and causes of failure (see text)

c. Drainage of SRF is not required because:
- The retina is freely mobile.
- The break can be apposed to the RPE without difficulty.
- The SRF is watery because the RD is fresh.

NB: Great care should be taken not to occlude the central retinal artery during a non-drainage procedure.

Long-standing retinal detachment

1. **Preoperative considerations.** Examination shows an extensive right 'macula-off' RD associated with a U-tear in the upper temporal quadrant and two small round holes in the lower temporal quadrant (Fig. 12.95a). A partially pigmented demarcation line is present at the junction of detached and flat retina, and a secondary intraretinal cyst is present inferiorly. This is therefore a long-standing RD because demarcation marks take about 3 months to develop and secondary retinal cysts usually take about 12 months. The prognosis for restoration of good visual acuity is poor because the macula has probably been detached for at least 12 months. There is therefore no urgency for surgery, which can be performed at the patient's and surgeon's convenience.
2. **Surgical technique**
   a. The peritomy should extend from 5.30 to 12.30 o'clock to expose the superior, lateral and inferior recti.
   b. The U-tear can be sealed with a 5 mm wide radial explant and the two holes with a 4 mm wide circumferential segmental explant (Fig. 12.95b). Alternatively, all breaks can be sealed with a long 4 mm wide circumferential segmental sponge explant extending from 7 to 10.30 o'clock (Fig. 12.95c).
   c. Drainage of SRF is required because the SRF is viscid and likely to take a long time to absorb.

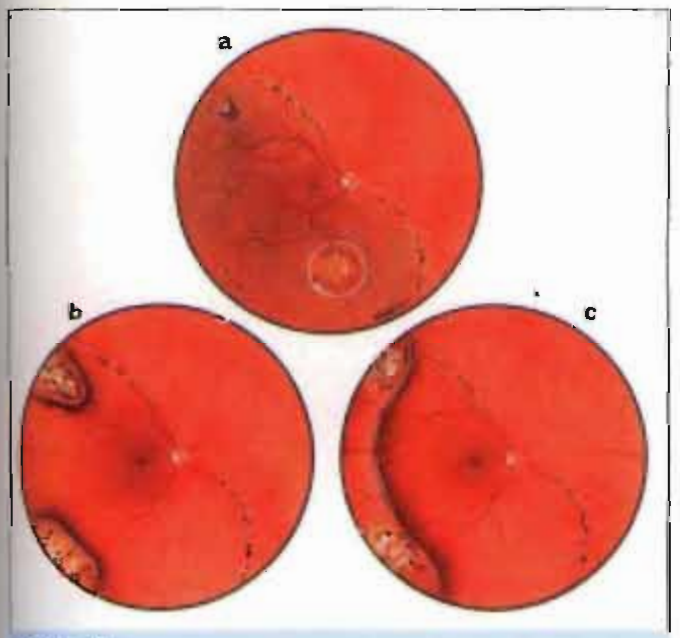

Fig. 12.95
Management of long-standing retinal detachment (see text)

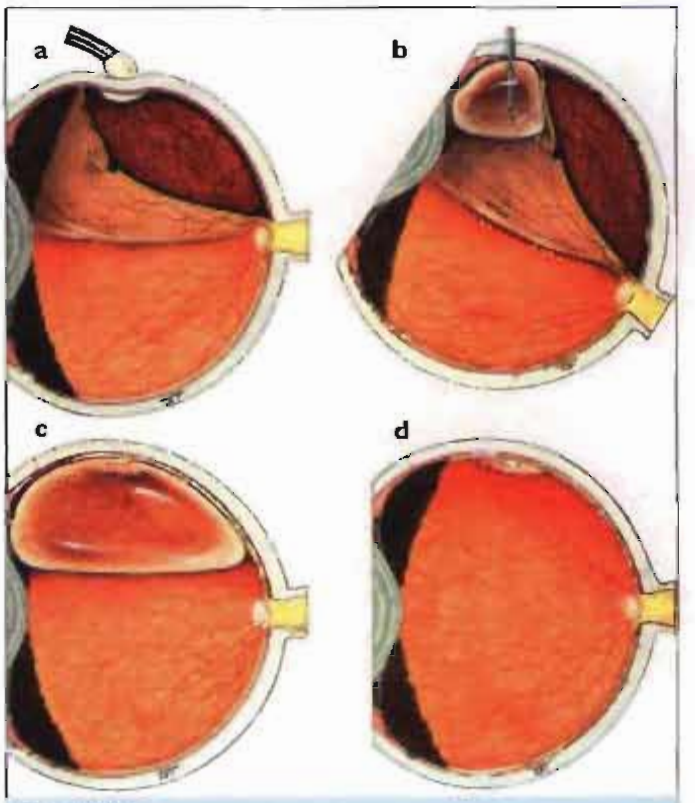

Fig. 12.96
Pneumatic retinopexy (see text)

Pneumatic retinopexy

Pneumatic retinopexy is an out-patient procedure in which an intravitreal expanding gas bubble is used to seal a retinal break and reattach the retina without scleral buckling. The most frequently used gases are sulphur hexafluoride (SF_6) and perfluoropropane (C_3F_8).

1. **Indications** are uncomplicated RDs with a small retinal break or a cluster of breaks extending over an area of less than two clock hours situated in the upper two-thirds of the peripheral retina.
2. **Surgical technique**
   a. Retinal breaks are treated with cryotherapy (Fig. 12.96a).
   b. An intravitreal injection is made of either 0.5 ml of 100% SF_6 or 0.3 ml of 100% C_3F_8 (Fig. 12.96b).
   c. Postoperatively, the patient is positioned so that the break is uppermost and the rising gas bubble remains in contact with the tear for 5–7 days (Fig. 12.96c and d).
   d. If required, additional cryotherapy or photocoagulation may be applied around the break.

Causes of failure

Early failure

This is most frequently due to the presence of an open break. The causes can be preoperative or operative.

Fig. 12.100
Erosion of sponge through lower lid

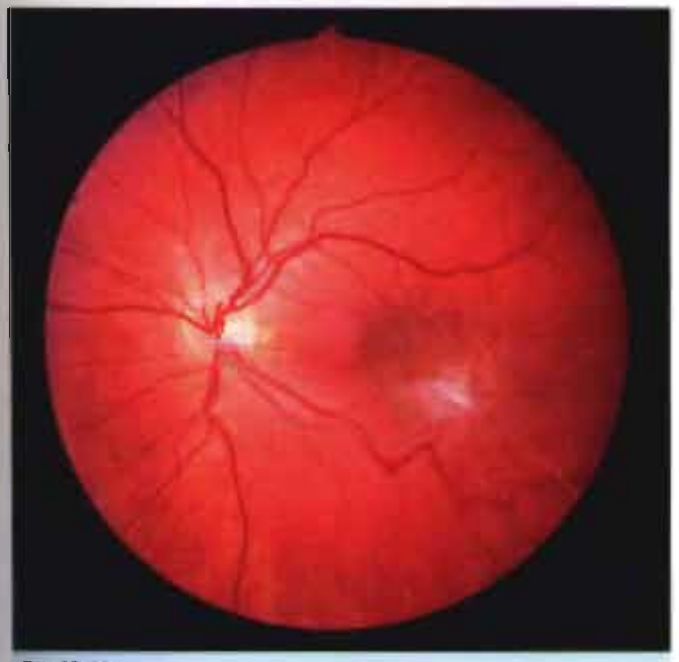

Fig. 12.101
Macular pucker

3. **Erosion** through the skin is very rare (Fig. 12.100).

Maculopathy

1. **Cellophane maculopathy** is characterized by an abnormal reflex at the macula, unassociated with distortion of the surrounding blood vessels. This finding is compatible with normal visual acuity.
2. **Macular pucker** is characterized by an opaque epiretinal membrane with distortion of blood vessels (Fig. 12.101). This complication appears unrelated to the type, extent or duration of RD, or to the type of surgical procedure. Most eyes with macular pucker have a visual acuity of less than 6/18.
3. **Pigmentary maculopathy** is usually the result of excessive cryotherapy.
4. **Atrophic maculopathy** is usually caused by the gravitation of blood in the subretinal space due to operative choroidal haemorrhage. This is seen in association with drainage of SRF since the needle track allows the blood to enter the subretinal space.

Diplopia

Transient diplopia is common during the immediate postoperative period and is a good prognostic sign indicating macular reattachment. Persistent diplopia is rare and may necessitate strabismus surgery or botulinum toxin injection. The following are the main predisposing factors:

- A large explant inserted under a rectus muscle. In most cases the diplopia resolves spontaneously after a few weeks or months and requires no specific therapy apart from reassurance or the temporary use of prisms. Very rarely a sponge may need to be removed.
- Surgical disinsertion of a rectus muscle (usually superior or inferior rectus) in order to place a buckle under it.
- Rupture of the muscle belly as a result of excessive traction on the sutures.
- Severe conjunctival scarring, usually associated with repeated operations, may cause mechanical restriction of eye movements.
- Decompensation of a large heterophoria resulting from poor postoperative visual acuity in the operated eye.

Pars plana vitrectomy

Introduction

Pars plana vitrectomy is a microsurgical procedure designed to remove vitreous gel, usually in order to gain access to a diseased retina. The most common approach is via three separate incisions through the pars plana.

Aims

1. **Excision of the posterior hyaloid face** (PHF) up to the posterior border of the vitreous base is of paramount importance in eyes with RD. The so-called 'core' vitrectomy which leaves the PHF and any associated retinal membranes intact is justifiable only in the management of endophthalmitis.
2. **Relief of vitreoretinal traction** by epiretinal membrane dissection and/or retinotomy.
3. **Retinal manipulation and reattachment.**
4. **Creation of a space** within the vitreous cavity for subsequent internal tamponade.
5. **Miscellaneous** aims, where appropriate, include removal of associated vitreous opacities, cataract, dislocated lens fragments or intraocular foreign bodies.

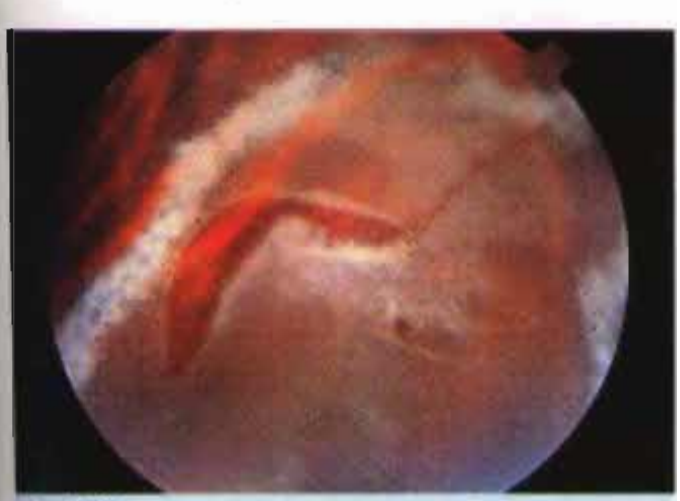

Fig. 12.105
Posterior retinal tear

- Cryotherapy or laser may be applied after retinal reattachment so that the amount of destructive energy is minimized.
- A tamponading agent ensures postoperative internal closure of retinal breaks.

2. **Complicated RDs** in which retinal breaks cannot be closed by conventional scleral buckling because of large size (Fig. 12.104), posterior location (Fig. 12.105) and association with PVR.

Tractional RD

1. **In proliferative diabetic retinopathy**, vitrectomy is indicated when RD involves or threatens the macula (*see* Chapter 14) and may be combined with internal panretinal laser photocoagulation. Combined tractional–rhegmatogenous RD should be treated urgently, even if the macula is not involved, because SRF is likely to spread quickly to involve the macula.
2. **In penetrating trauma**, vitrectomy is aimed at visual rehabilitation and minimizing the tractional process predisposing to RD.

Techniques

Proliferative vitreoretinopathy

The aims of surgery include release of transvitreal traction by vitrectomy and tangential (surface) traction by membrane dissection in order to restore retinal mobility and allow closure of retinal breaks.

1. **Initial steps**
   a. The infusion cannula is secured to an inferotemporal sclerotomy 3.5 mm behind the limbus.
   b. Two further sclerotomies are made at the 10 and 2 o'clock positions, through which the cutter and the fibre-optic light pipe are inserted (Fig. 12.106).
   c. The central vitreous gel and posterior hyaloid face are excised.

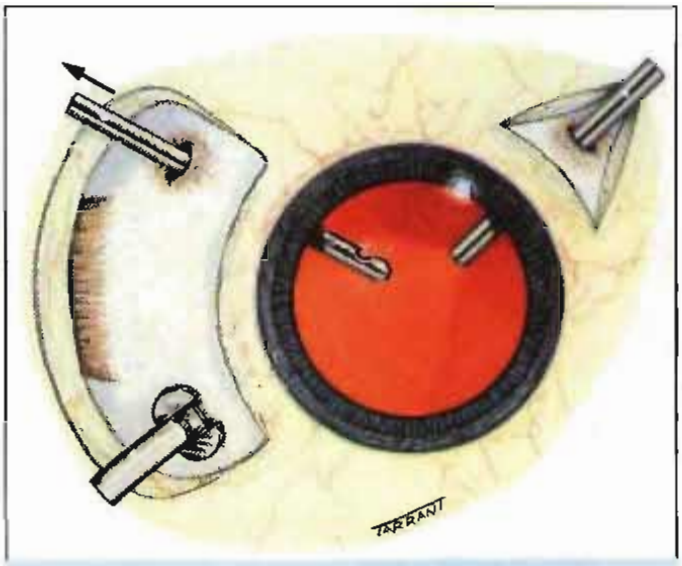

Fig. 12.106
Infusion cannula, light pipe and vitreous cutter in position

Fig. 12.107
Dissection of starfolds in proliferative vitreoretinopathy

2. **Membrane dissection** of localized fixed retinal (star) folds is as follows:
   a. The tip of a vertically cutting scissors is engaged in the membrane at the edge of the valley between two adjacent retinal folds (Fig. 12.107) and the membrane is pulled towards the ora serrata until it peels from the surface of the retina.
   b. Internal fluid–air exchange is performed and retinopexy applied to retinal breaks.
   c. The vitreous base is supported by a broad scleral buckle.
   d. The intraocular air is exchanged for an extended intraocular tamponading agent such as C_3F_8 or silicone oil.

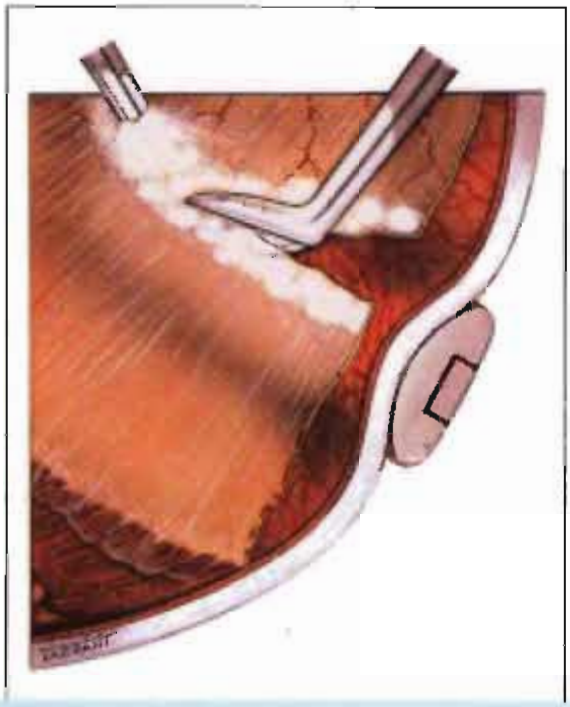

Fig. 12.108
Relieving retinotomy in proliferative vitreoretinopathy

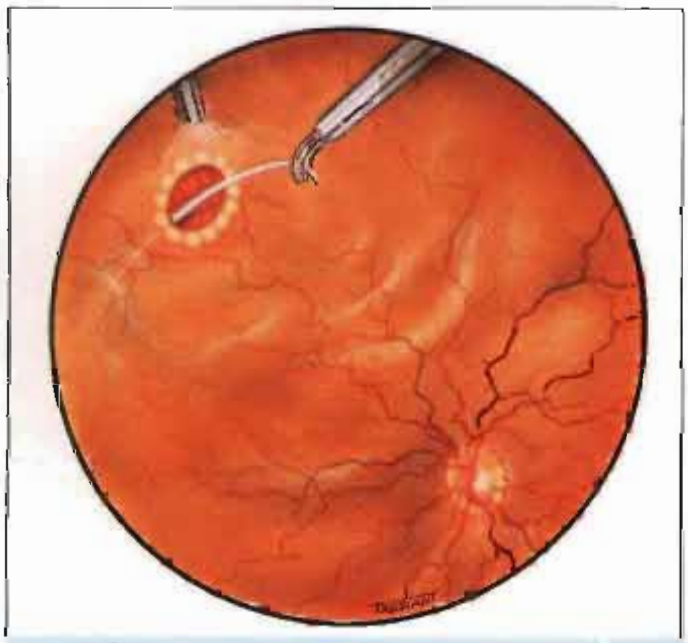

Fig. 12.109
Removal of a subretinal membrane in proliferative vitreoretinopathy

3. **Relieving retinotomy** may be required after membrane dissection if retinal mobility is deemed insufficient for lasting reattachment (Fig. 12.108).
4. **Removal of subretinal membranes** may be required in selected cases (Fig. 12.109).

Tractional retinal detachment

The aims of surgery are to release anteroposterior and/or circumferential vitreoretinal traction. Since the membranes are vascularized they cannot be simply peeled from the surface of the retina as in PVR because this would result in haemorrhage and tearing of the retina. Fibrovascular membranes in diabetic tractional RDs may be removed by:

1. **Delamination**, which involves the horizontal cutting of the individual vascular pegs connecting the membranes to the surface of the retina (Fig. 12.110). This is preferable to segmentation because it allows the complete removal of fibrovascular tissue from the retinal surface (en-bloc delamination).
2. **Segmentation** involves the vertical cutting of epiretinal membranes into small segments (Fig. 12.111). It is used to release circumferential vitreoretinal traction when delamination is difficult or impossible, such as in very mobile combined tractional–rhegmatogenous RD associated with posterior retinal breaks.

Postoperative complications

1. **Raised intraocular pressure** may be caused by the following mechanisms:
   - Overexpansion of intraocular gas.

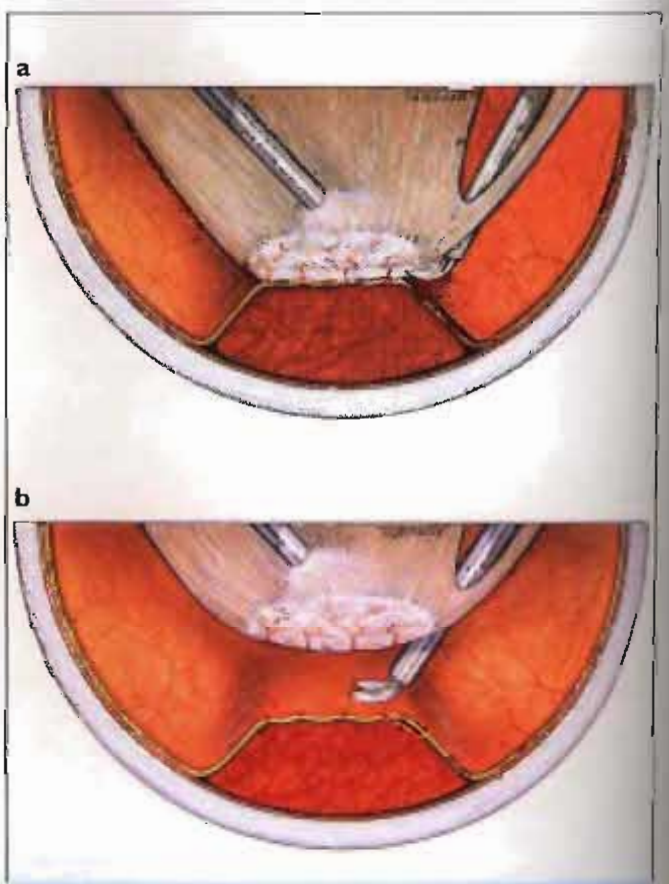

Fig.12.110
(a) Delamination with horizontally cutting scissors; (b) delamination completed

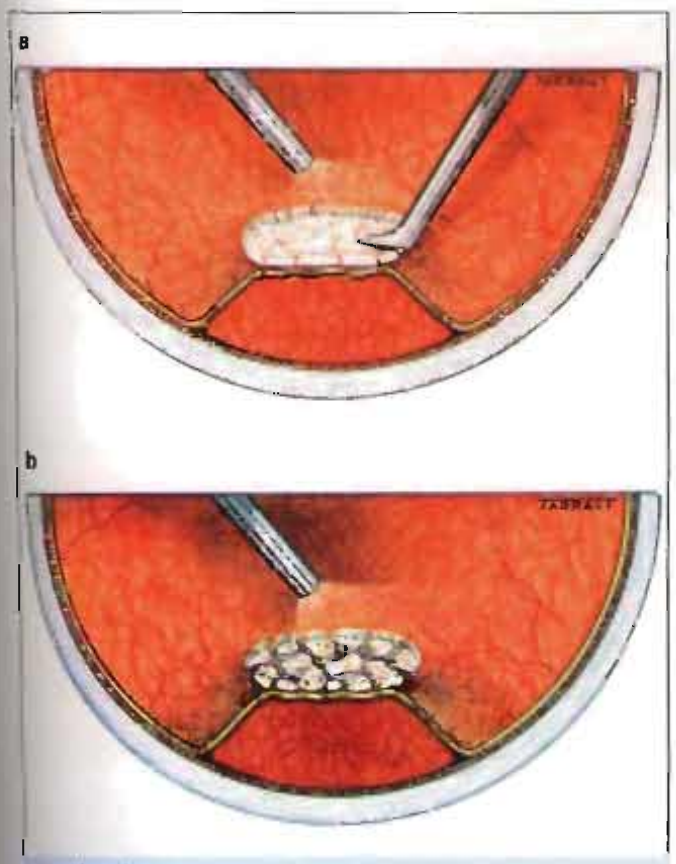

Fig. 12.111
(a) Segmentation with vertically cutting scissors; (b) segmentation completed

Fig. 12.113
Emulsified silicone oil in the anterior chamber

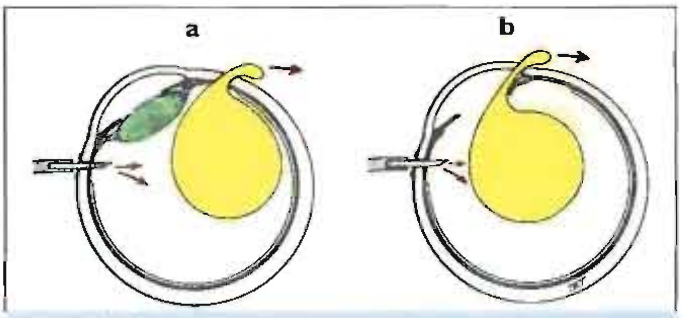

Fig. 12.114
Removal of silicone oil. (a) In phakic eye; (b) in aphakic eye

Fig. 12.112
Silicone oil in the anterior chamber

Fig. 12.115
Induced cataract and emulsified silicone oil

- Early silicone-oil-induced glaucoma is caused by oil in the anterior chamber (Fig. 12.112).
- Late silicone-oil-induced glaucoma is probably due to trabecular blockage by emulsified oil in the anterior chamber (Fig. 12.113). This may be prevented by early removal of silicone oil either via the pars plana in the phakic eye or the limbus in the aphakic eye (Fig. 12.114).
- Ghost cell or steroid-induced glaucoma.

2. **Cataract** may be caused by the following:
   - Gas-induced lens opacities are usually transient and can be minimized by using lower concentrations and smaller volumes of gas.
   - Silicone-oil-induced lens opacities (Fig. 12.115) develop in almost all phakic eyes. If a cataract develops, the silicone oil may be removed in conjunction with cataract surgery.

- Delayed nuclear sclerosis almost invariably develops within 5–10 years.

3. **Retinal re-detachment** occurs most commonly when the intraocular gas bubble has absorbed (3–6 weeks postoperatively), or following removal of silicone oil. The main causes are:
   - Reopening of the original break because of inadequate operative dissection in eyes with PVR or re-proliferation of epiretinal membranes, more common in eyes with proliferative diabetic retinopathy.
   - New or missed breaks, especially those related to the pars plana sclerotomy sites.

> ***NB:*** Early removal of silicone oil is associated with a 25% risk of retinal re-detachment in eyes with PVR and giant tears, and 11% risk in eyes with proliferative diabetic retinopathy

CHAPTER 13

Acquired Macular Disorders

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Introduction

Applied anatomy

Landmarks (Figs 13.1 and 13.2)

1. **The macula** is a round area at the posterior pole measuring approximately 5.5 mm in diameter. Histologically, it contains xanthophyll pigment and more than one layer of ganglion cells.
2. **The fovea** is a depression in the inner retinal surface at the centre of the macula with a diameter of 1.5 mm (about one disc) (Fig. 13.3). Ophthalmoscopically it gives rise to an oval light reflex (Fig. 13.4) because of the increased thickness of the retina and internal limiting membrane at its border.
3. **The foveola** forms the central floor of the fovea and has a diameter of 0.35 mm. It is the thinnest part of the retina, is devoid of ganglion cells and consists only of cones and their nuclei.
4. **The foveal avascular zone** (FAZ) is located within the fovea but extends beyond the foveola. The exact diameter is variable and its location can be determined with accuracy only by fluorescein angiography (Fig. 13.5).
5. **The umbo** is a tiny depression in the very centre of the foveola which corresponds to the foveolar reflex, loss of which may be an early sign of damage.

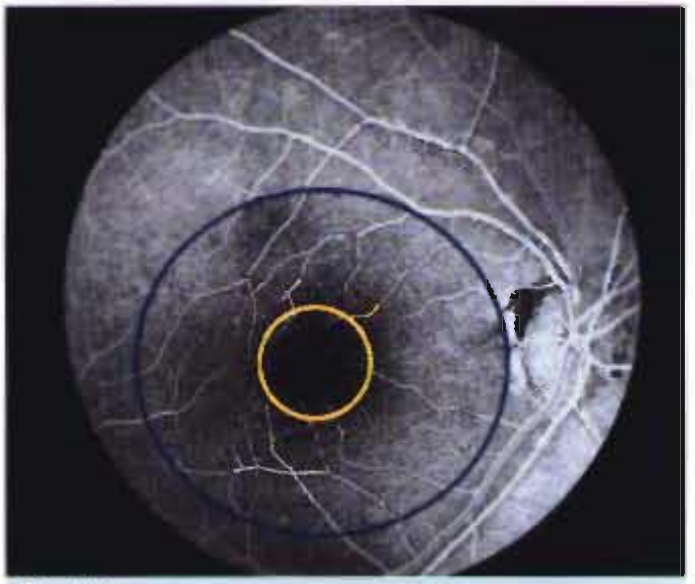


Fig. 13.1
Anatomical landmarks. Macula (blue circle); fovea (yellow circle)

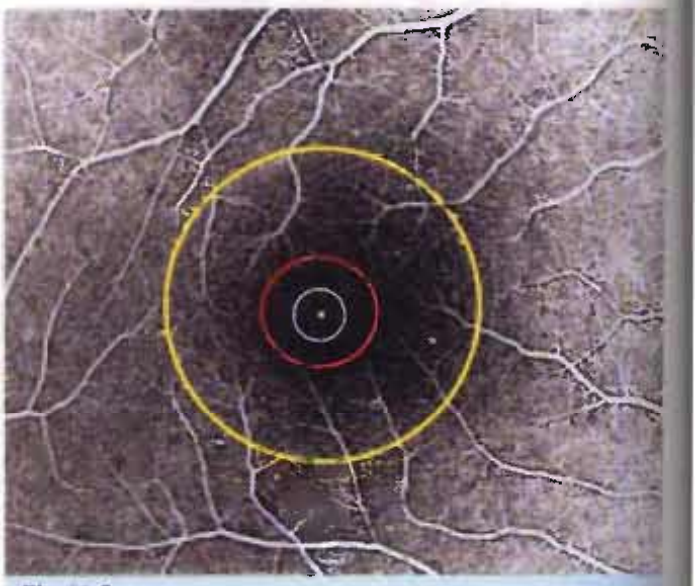


Fig. 13.2
Anatomical landmarks. Fovea (yellow circle); foveal avascular zone (red circle); foveola (lilac circle); umbo (central white spot)

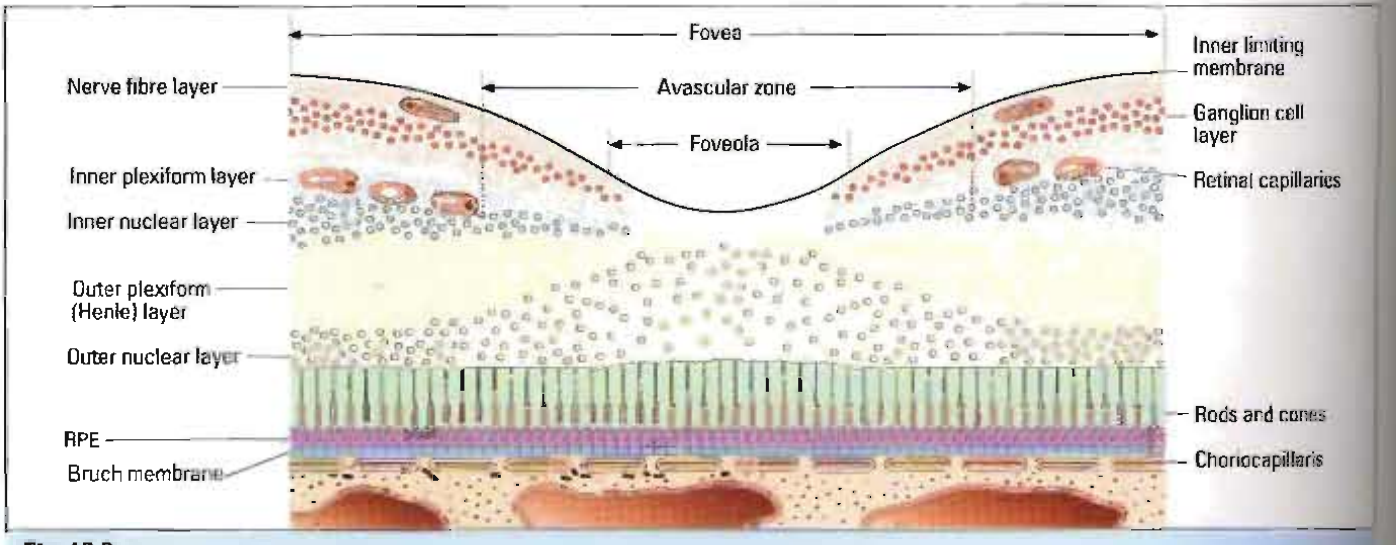


Fig. 13.3
Cross-section of the fovea

Fig. 13.4
Normal foveal light reflex

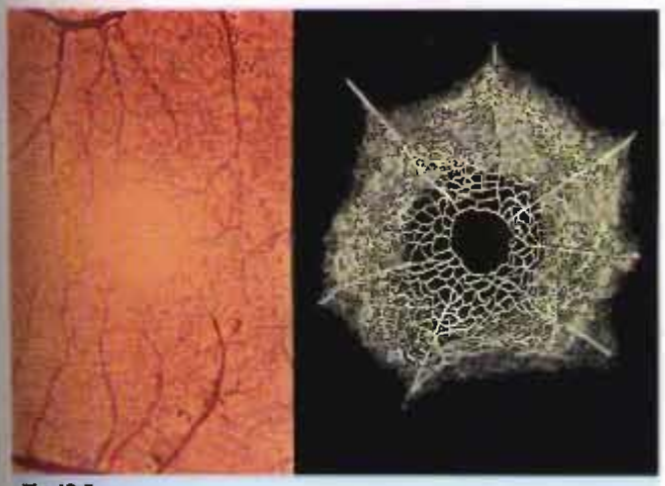


Fig. 13.5
Foveal avascular zone (Courtesy of Wilmer Eye Institute)

Retinal pigment epithelium (RPE)

The retinal pigment epithelium (RPE) is a single layer of hexagonal cells, the apices of which manifest villous processes that envelop the outer segments of the photoreceptors. The RPE cells at the fovea are taller, thinner and contain more and larger melanosomes than elsewhere in the retina. The adhesion between the RPE and sensory retina is weaker than between the RPE and Bruch membrane, which underlies the RPE. The potential space between the RPE and sensory retina is the subretinal space. The RPE maintains the integrity (i.e. dryness) of the subretinal space in two ways:

- The RPE cells and the intervening tight junctional complexes (zonula occludentes) constitute the outer blood–retinal barrier (*see* Fig. 13.12), which prevents extracellular fluid, which normally leaks from the choriocapillaris from entering the subretinal space.
- It also actively pumps ions and water out of the subretinal space.

Bruch membrane

This separates the RPE from the choriocapillaris. On electron microscopy it consists of five elements:

- Basal lamina of the RPE.
- Inner collagenous layer.
- Thicker band of elastic fibres.
- Outer collagenous layer.
- Basal lamina of the outer layer of the choriocapillaris.

Changes in Bruch membrane are relevant to the pathogenesis of many macular disorders.

Clinical evaluation

Symptoms

1. **Impairment of central vision** is the main symptom. Patients with macular disease complain of 'something obstructing central vision' (positive scotoma) in contrast with those with optic neuropathy, who may notice a hole in their vision (negative scotoma).
2. **Metamorphopsia**, distortion of perceived images, is a common symptom not present in optic neuropathy.
3. **Micropsia**, a decrease in image size caused by spreading apart of foveal cones, is less common.
4. **Macropsia**, an increase in image size due to crowding together of foveal cones, is uncommon.

> *NB:* Colour desaturation is not present in mild macular disease, but is common in early optic nerve disease.

Clinical examination

1. **Visual acuity** is the most important test of macular function, particularly for near. In patients with macular

Fig. 13.6
Slit-lamp indirect biomicroscopy

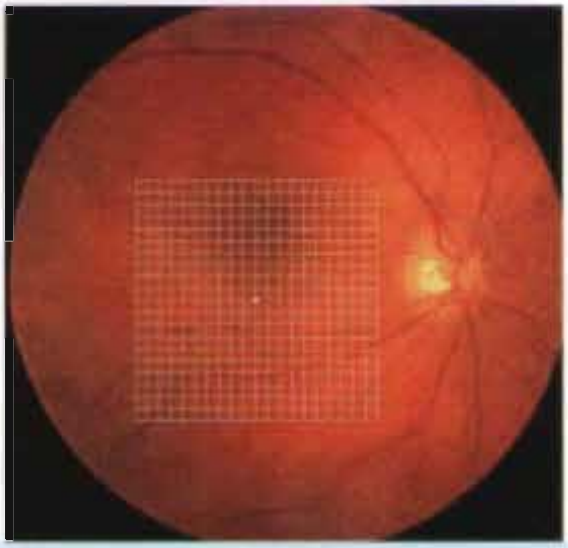


Fig. 13.7
Amsler grid superimposed on the retina (Courtesy of A. Franklin)

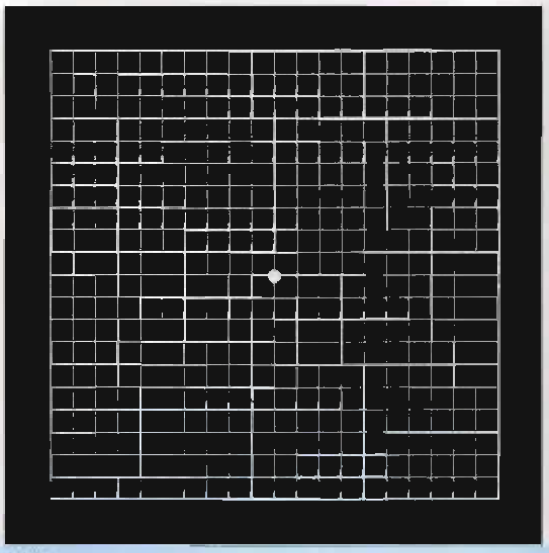


Fig. 13.8
Amsler grid chart 1 (Courtesy of A. Franklin)

disease visual acuity is frequently worse when the patient looks through a pinhole.

2. **Slit-lamp indirect biomicroscopy** with a contact lens or a strong convex lens affords excellent visualization of the macula (Fig. 13.6). Monochromatic light is useful in detecting subtle lesions which may otherwise be overlooked. Green (red-free) light may also enhance detection of superficial retinal lesions such as wrinkling of

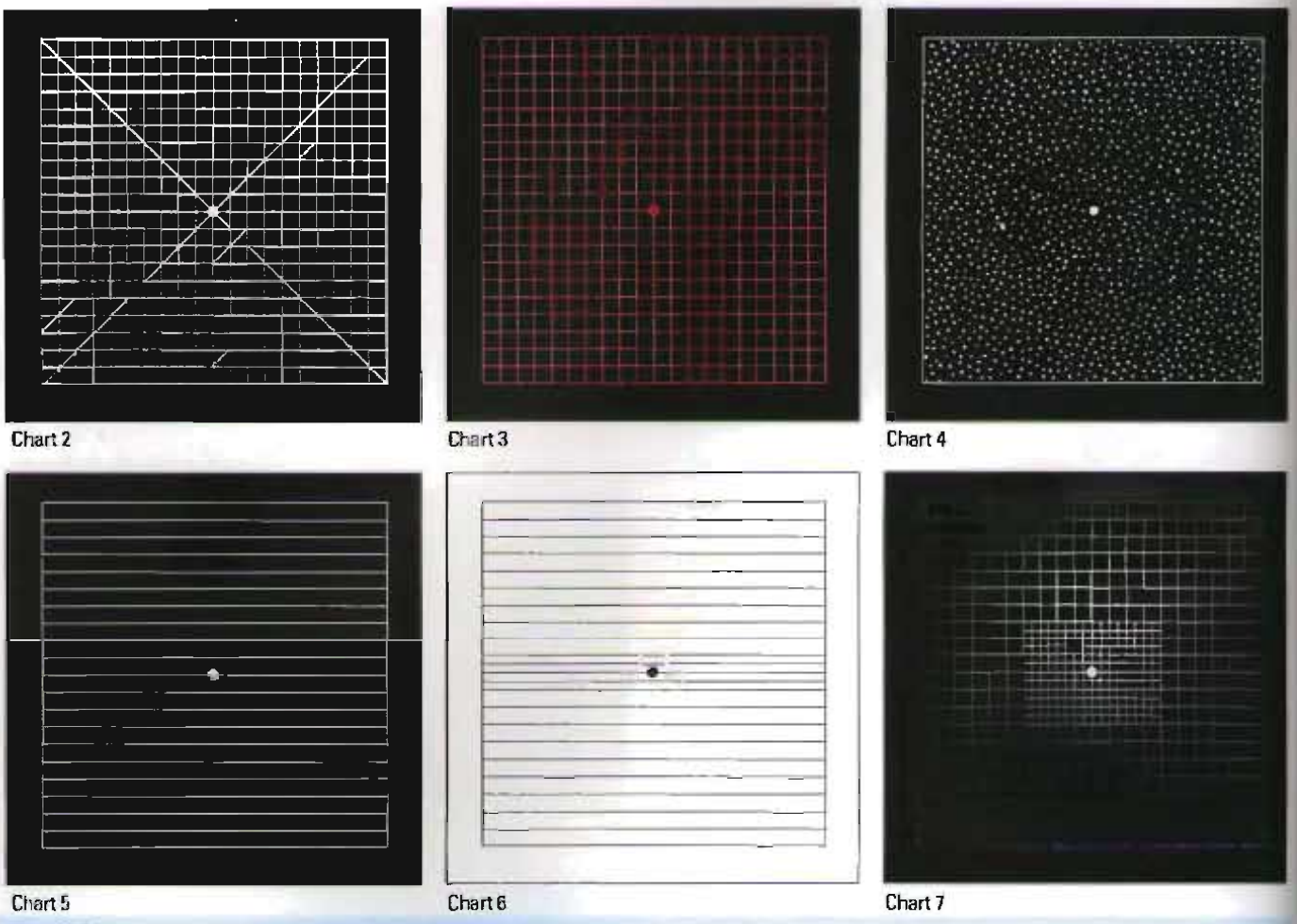


Fig. 13.9
Amsler grid charts 2–7 (Courtesy of A. Franklin)

the internal limiting membrane or cystoid oedema. It is also useful in delineating the outline of subtle serous elevations of the sensory retina. Lesions involving the RPE and choroid are best detected using light at the red end of the spectrum.

3. **Amsler grid** testing evaluates the 10° of the visual field surrounding fixation (Fig. 13.7) and is useful for both screening and monitoring macular disease. There are seven charts, each consisting of a 10 cm square (Figs 13.8 and 13.9).
   a. *Chart 1* is divided into 400 smaller 5 mm squares. When viewed at one-third of a metre, each small square subtends an angle of 1°.
   b. *Chart 2* is similar to chart 1 but has diagonal lines that aid fixation in patients unable to see the central spot.
   c. *Chart 3* is identical to chart 1 but has red squares which may be helpful in detecting colour desaturation in patients with optic nerve lesions.
   d. *Chart 4* consisting of random dots is seldom used.
   e. *Chart 5* consists of horizontal lines and is designed to detect metamorphopsia along specific meridia, especially horizontally to investigate difficulties with reading.
   f. *Chart 6* is similar to chart 5 but has a white background and the central lines are closer together.
   g. *Chart 7* exhibits a fine central grid, each square subtending an angle of 1/2° and is therefore more sensitive.

   The test is performed as follows:
   a. The patient wears reading spectacles, if appropriate, and covers one eye.
   b. The patient is asked to look directly at the centre dot with the uncovered eye and report any distortion, blurred areas or blank spots anywhere on the grid.
   c. Patients with maculopathy often report that the lines are wavy whereas those with optic neuropathy often remark that some of the lines are missing or faint but not distorted (Fig. 13.10).
4. **Photostress testing** may be useful to detect maculopathy when ophthalmoscopy is equivocal and also to differentiate macular disease from optic neuropathy. It is performed as follows:
   a. The best corrected distance visual acuity is determined.
   b. The patient fixates the light of a pen-torch or an indirect ophthalmoscope held about 3 cm away for about 10 seconds.
   c. The photostress recovery time (PSRT) is the time taken to read any three letters of the pre-test acuity line and is normally between 15 and 30 seconds.
   d. The test is performed on the other, presumably normal, eye and the results are compared.

   The PSRT is prolonged, relative to the normal eye, in macular disease (sometimes 50 seconds or more) but not in optic neuropathy.
5. **Pupillary light reactions** are usually normal in eyes with macular disorders, in contrast to mild lesions of the optic nerve, in which a relative afferent pupillary defect occurs early (*see* Chapter 18).

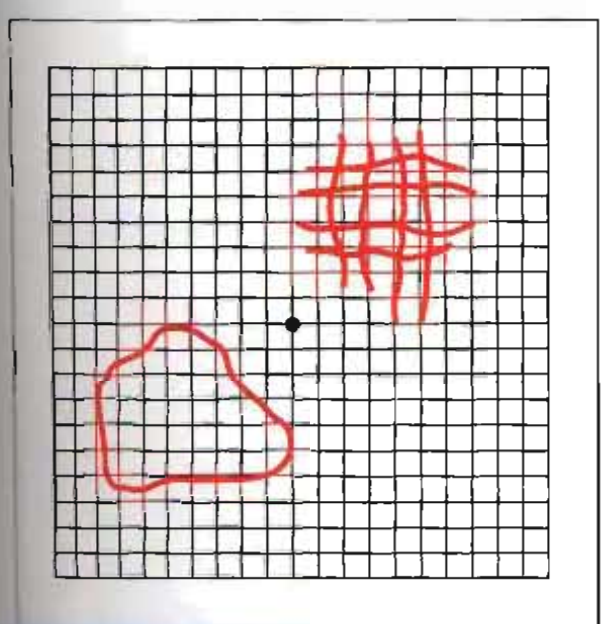


Fig. 13.10
Amsler recording chart on which a patient has drawn to indicate metamorphopsia and a relative scotoma (Courtesy of A Franklin)

Fundus angiography

Fluorescein angiography

General principles

1. **Fluorescein** is an orange water-soluble dye that when injected intravenously remains largely intravascular and circulates in the bloodstream.
2. **Fluorescein angiography** (FA) involves photographic surveillance of the passage of fluorescein through the retinal and choroidal circulations.
3. **Fluorescein binding.** On intravenous injection, between 70% and 85% of fluorescein molecules bind to serum proteins (bound fluorescein); the remainder remain unbound (free fluorescein) (Fig. 13.11).
4. **The outer blood–retinal barrier.** The major choroidal vessels are impermeable to both bound and free fluorescein. However, the walls of the choriocapillaris are extremely thin and contain multiple fenestrations (Fig. 13.12a) through which free fluorescein molecules escape into the extravascular space, from which they pass across Bruch membrane. However, on reaching the RPE, they encounter tight junctional intercellular complexes termed zonula occludentes, which prevent the passage of free fluorescein molecules across the RPE (Fig. 13.12b).

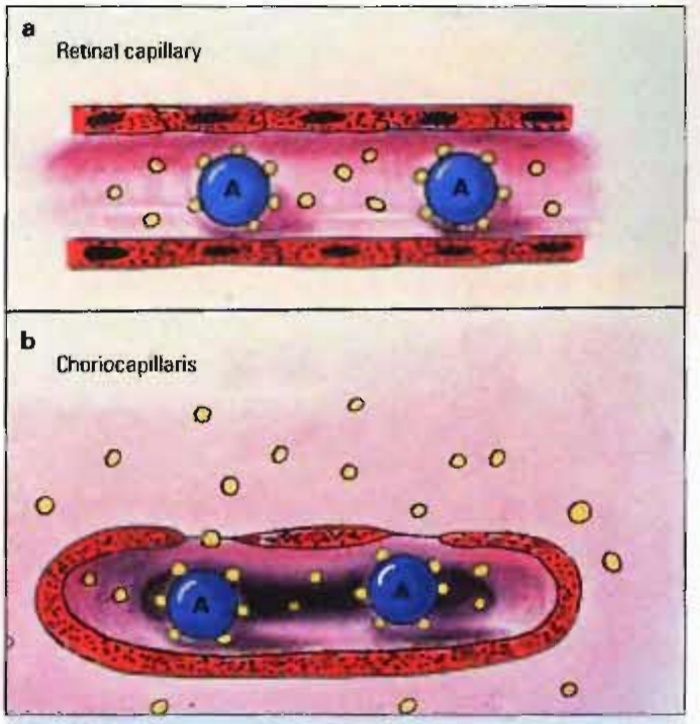


Fig. 13.11
Fluorescein binding and permeability (A = albumin) (see text) (Courtesy of Wilmer Institute)

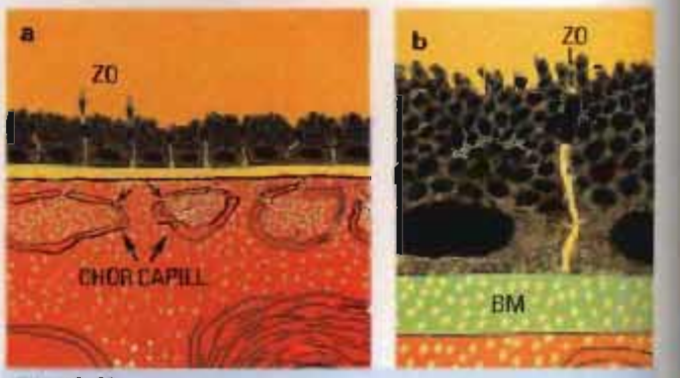


Fig. 13.12
Outer blood–retinal barrier (ZO = zonula occludentes; BM = Bruch membrane) (see text) (Courtesy of Wilmer Institute)

5. **The inner blood–retinal barrier** is composed of the tight junctions between retinal capillary endothelial cells across which neither bound nor free fluorescein can pass (Fig. 13.13a and b). Fluorescein is therefore confined to within the lumen of the retinal capillaries. The basement membrane and pericytes play only a minor role in this regard. Disruption of the inner blood–retinal barrier will permit leakage of both bound and free fluorescein molecules into the extravascular space (Fig. 13.13c and d).

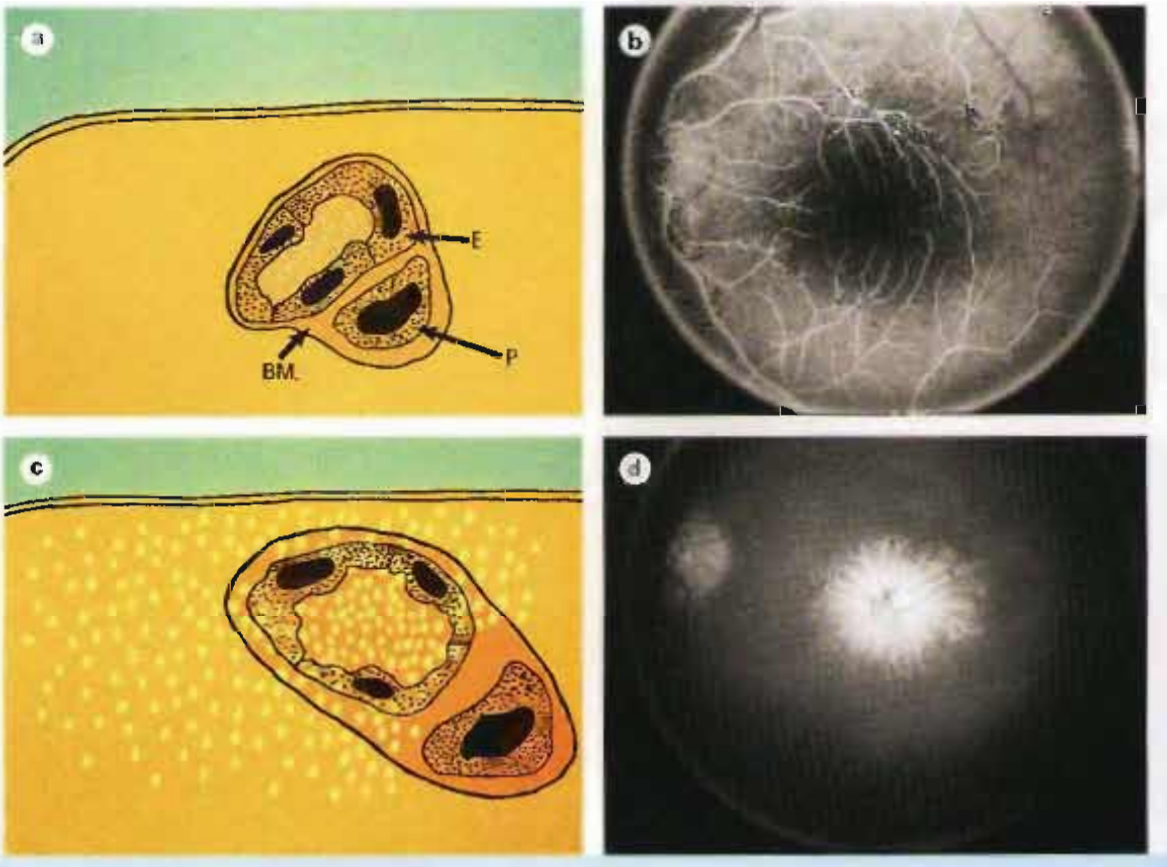


Fig. 13.13
Inner blood–retinal barrier. (a) Intact barrier without leakage of fluorescein (BM = basement membrane, P = pericyte, E = endothelial cell); (b) FA showing absence of leakage; (c) disrupted barrier with leakage of fluorescein; (d) FA showing leakage (Courtesy of Wilmer Institute)

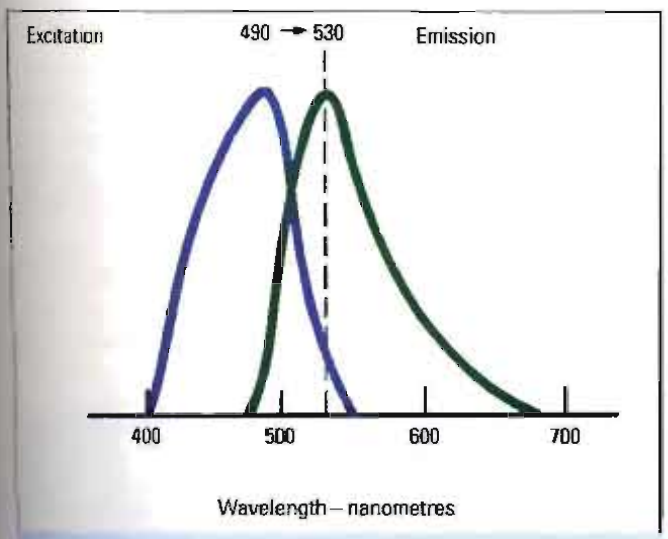


Fig. 13.14
Excitation and emission of fluorescence

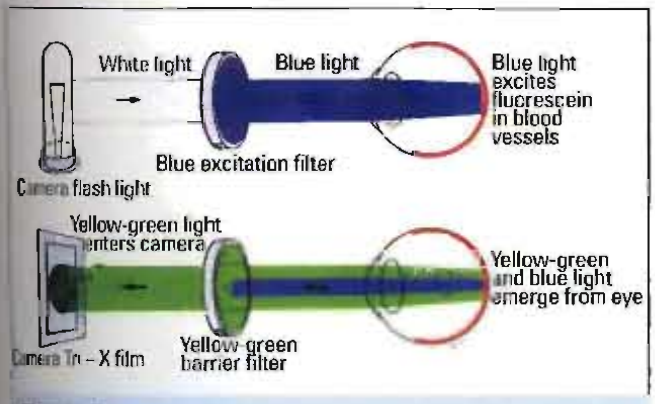


Fig. 13.15
Photographic principles of FA

Fig. 13.16
Position of patient for FA

6. **Fluorescence** is the property of certain molecules to emit light energy of a longer wavelength when stimulated by light of a shorter wavelength (Fig. 13.14). The excitation peak for fluorescein is about 490 nm (blue part of the spectrum) and represents the maximal absorption of light energy by fluorescein. Molecules stimulated by this wavelength will be excited to a higher energy level and will emit light of a longer wavelength (green part of the spectrum) at about 530 nm.
7. **Filters** of two types are used to ensure that blue light enters the eye and only yellow-green light enters the camera (Fig. 13.15).
   *a. A **blue excitation** filter through which passes white light from the camera flash. The emerging blue light enters the eye and excites the fluorescein molecules in the retinal and choroidal circulations, which then emit light of a longer wavelength (yellow-green).*
   *b. A **yellow-green barrier** filter then blocks any reflected blue light from the eye, allowing only yellow-green light to pass through unimpaired to be recorded on film.*

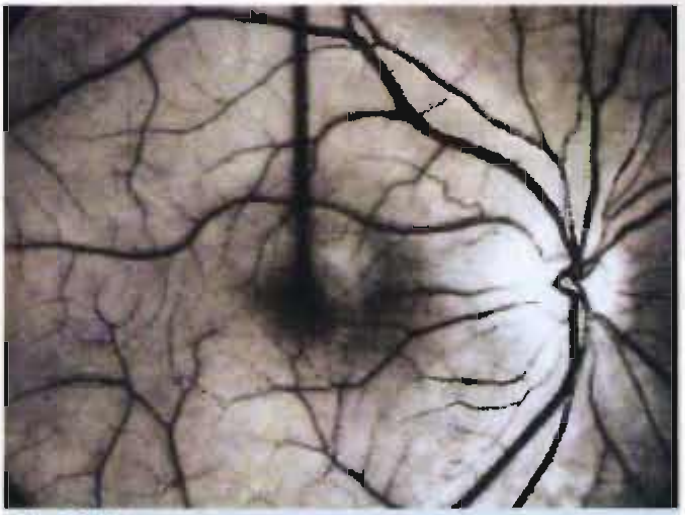


Fig. 13.17
Red-free photograph

Photographic technique

A good-quality angiogram requires adequate pupillary dilatation and clear media.

1. The patient is seated in front of the fundus camera (Fig. 13.16).
2. Fluorescein, usually 5 ml of a 10% solution, is drawn up into a syringe. In eyes with opaque media, 3 ml of a 25% solution may afford better results.
3. A 'red-free' photograph is taken (Fig. 13.17).
4. Fluorescein is injected rapidly intravenously.
5. Photographs are taken at approximately 1-second intervals, 5–25 seconds after injection.
6. After the transit phase has been photographed in one eye, control pictures are taken of the opposite eye. If appropriate, late photographs may also be taken after 10 minutes and, occasionally, 20 minutes if leakage is anticipated.

Adverse effects

Discoloration of skin and urine is almost universal. Mild side effects include nausea, vomiting, flushing of the skin, itching, hives and excessive sneezing. Serious but rare problems

include syncope, laryngeal oedema, bronchospasm and anaphylactic shock.

> ***NB:*** It is very important to have arrangements for managing these eventualities.

Phases of the angiogram

Fluorescein enters the eye through the ophthalmic artery, passing into the choroidal circulation through the short posterior ciliary arteries and into the retinal circulation through the central retinal artery. Because the route to the retinal circulation is slightly longer than that to the choroidal, the latter is filled about 1 second before the former (Fig. 13.18). In the choroidal circulation, precise details are often not discernible, mainly because of rapid leakage of free fluorescein from the choriocapillaris and also because the melanin in the RPE cells blocks choroidal fluorescence. The angiogram consists of the following overlapping phases: (a) *choroidal (pre-arterial)*, (b) *arterial*, (c) *arteriovenous (capillary)* and (d) *venous* (Fig. 13.19).

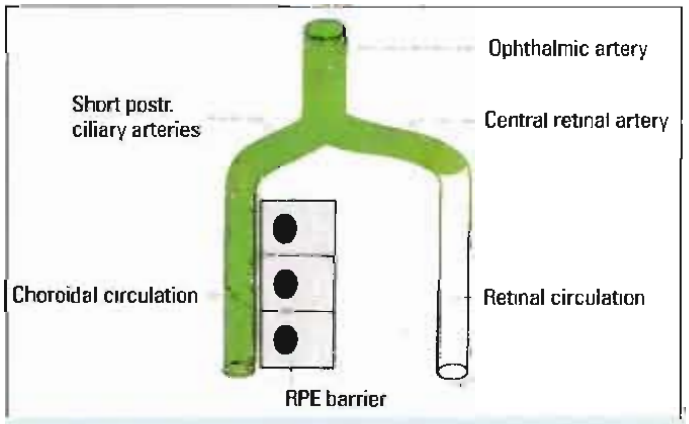


Fig. 13.18
Entry of fluorescein into the choroidal and retinal circulations

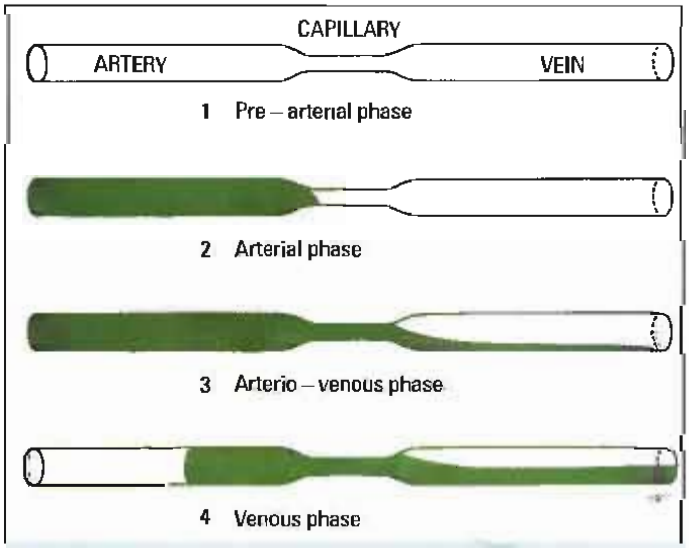


Fig. 13.19
Four phases of the fluorescein angiogram

The normal angiogram

1. **The choroidal (pre-arterial) phase** occurs 8–12 seconds after dye injection and is characterized by patchy filling of the choroid due to leakage of free fluorescein through the fenestrated choriocapillaris. A cilioretinal artery, if present, will fill at this time (Fig. 13.20) because it is derived from the posterior ciliary circulation.
2. **The arterial phase** shows arterial filling and the continuation of choroidal filling (Fig. 13.21).

Fig. 13.20
Choroidal phase showing patchy choroidal filling and filling of a cilioretinal artery

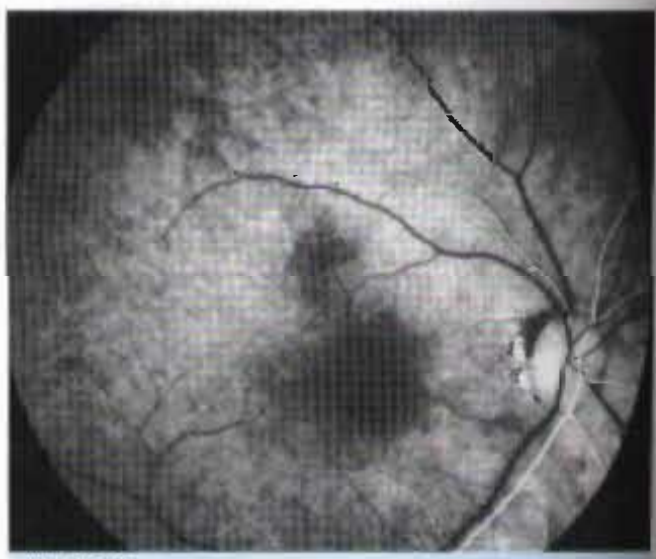


Fig. 13.21
Arterial phase showing filling of the choroid and retinal arteries

3. **The arteriovenous (capillary) phase** shows complete filling of the arteries and capillaries with early laminar flow in the veins in which the dye is seen along the lateral wall of the vein (Fig. 13.22). Choroidal filling continues and background choroidal fluorescence increases as free fluorescein continues to leak from the choriocapillaris into the extravascular space. In hypopigmented eyes, this may be so marked that details of the retinal capillaries may be obscured. In highly pigmented eyes, background choroidal fluorescence will be less obvious.
4. **The venous phase**
   a. *The early* phase exhibits complete arterial and capillary filling, and more marked laminar venous flow (Fig. 13.23).
   b. *The mid* phase displays almost complete venous filling (Fig. 13.24).
   c. *The late* phase shows complete venous filling with reducing concentration of dye in the arteries.
5. **The late (elimination) phase** demonstrates the effects of continuous recirculation, dilution and elimination of the dye. With each succeeding wave, the intensity of fluorescence becomes weaker. Late staining of the disc is a normal finding (Fig. 13.25). Fluorescein is absent from the angiogram after 5–10 min and is usually totally eliminated from the body within several hours.

Dark appearance of the fovea

The dark appearance of the fovea on FA (Fig. 13.26a) is caused by three phenomena (Fig. 13.26b):

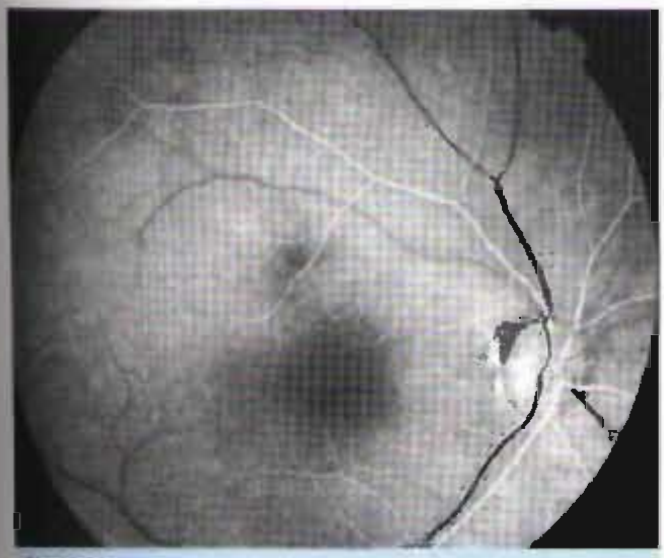


Fig. 13.22
Arteriovenous (capillary) phase showing complete arterial filling and early lamellar venous flow

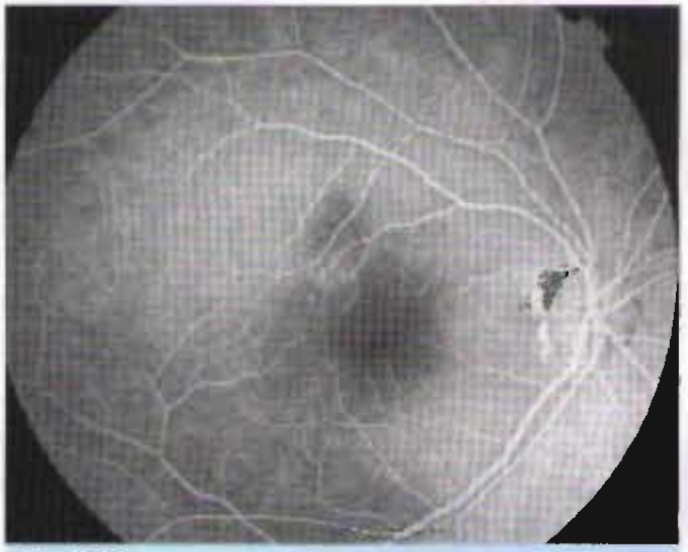


Fig. 13.24
Mid venous phase showing almost complete venous filling

Fig. 13.23
Early venous phase showing marked lamellar venous flow

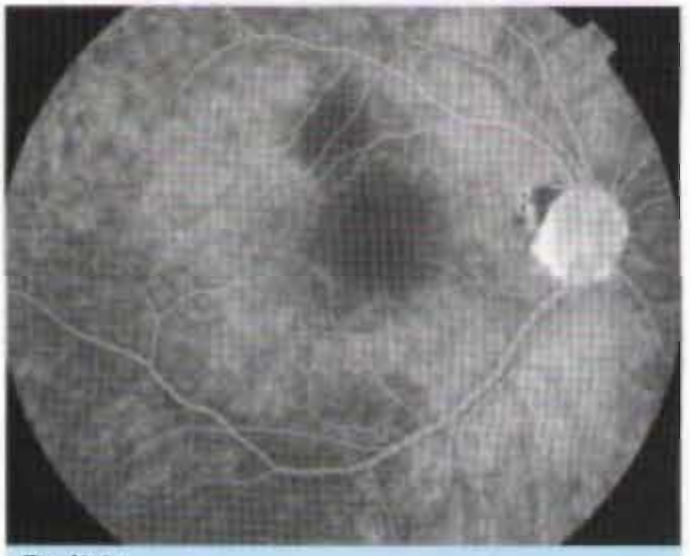


Fig. 13.25
Late (elimination) phase showing weak fluorescence and staining of the optic disc

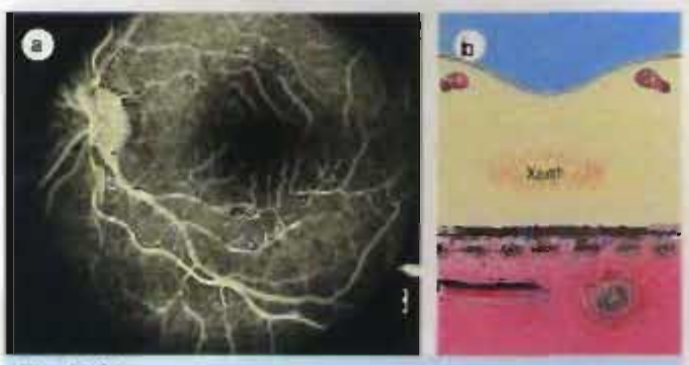


Fig. 13.26
Dark appearance of the fovea on FA (Xanth = xanthophil) (see text) (Courtesy of Wilmer Institute)

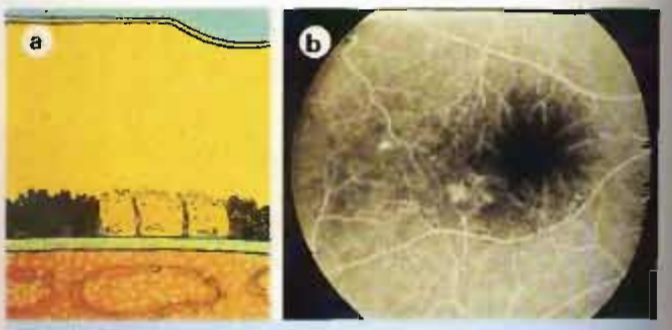


Fig. 13.27
Hyperfluorescence due to a pigment epithelial window defect (see text) (Courtesy of Wilmer Institute)

- Avascularity of FAZ.
- Blockage of background choroidal fluorescence due to increased density of xanthophyll at the fovea.
- Blockage of background choroidal fluorescence by the RPE cells at the fovea, which are large and contain more melanin than those elsewhere.

Causes of hyperfluorescence

Increased fluorescence may be due to enhanced visualization of a normal quantity of fluorescein in the fundus, or an absolute increase in the fluorescein content of the tissues.

1. **A transmission (window) defect** results from focal RPE atrophy (Fig. 13.27a) or absence, with resultant unmasking of normal background choroidal fluorescence (Fig. 13.27b). It is characterized by early hyperfluorescence which increases in intensity and then fades without changing size or shape.
2. **Pooling** of dye in an anatomical space may occur due to breakdown of the outer blood–retinal barrier (RPE tight junctions).
   *a. **In the subretinal space*** (Fig. 13.28b), as in central serous retinopathy (Fig. 13.28a), it is characterized by early hyperfluorescence (Fig. 13.28c) which increases in both size and intensity (Fig. 13.28d–f).
   *b. **In the sub-RPE space*** (Fig. 13.29b), as in pigment epithelial detachment (PED) (Fig. 13.29a), it is characterized by early hyperfluorescence (Fig. 13.29c) which increases in intensity but not in size (Fig. 13.29d).
3. **Leakage** of dye may occur from:
   *a. **Abnormal choroidal vasculature***, such as choroidal neovascularization (CNV) (Fig. 13.30a), is characterized by an early lacy filling pattern of hyperfluorescence (Fig. 13.30b) which increases in size and intensity (Fig. 13.30c and d).

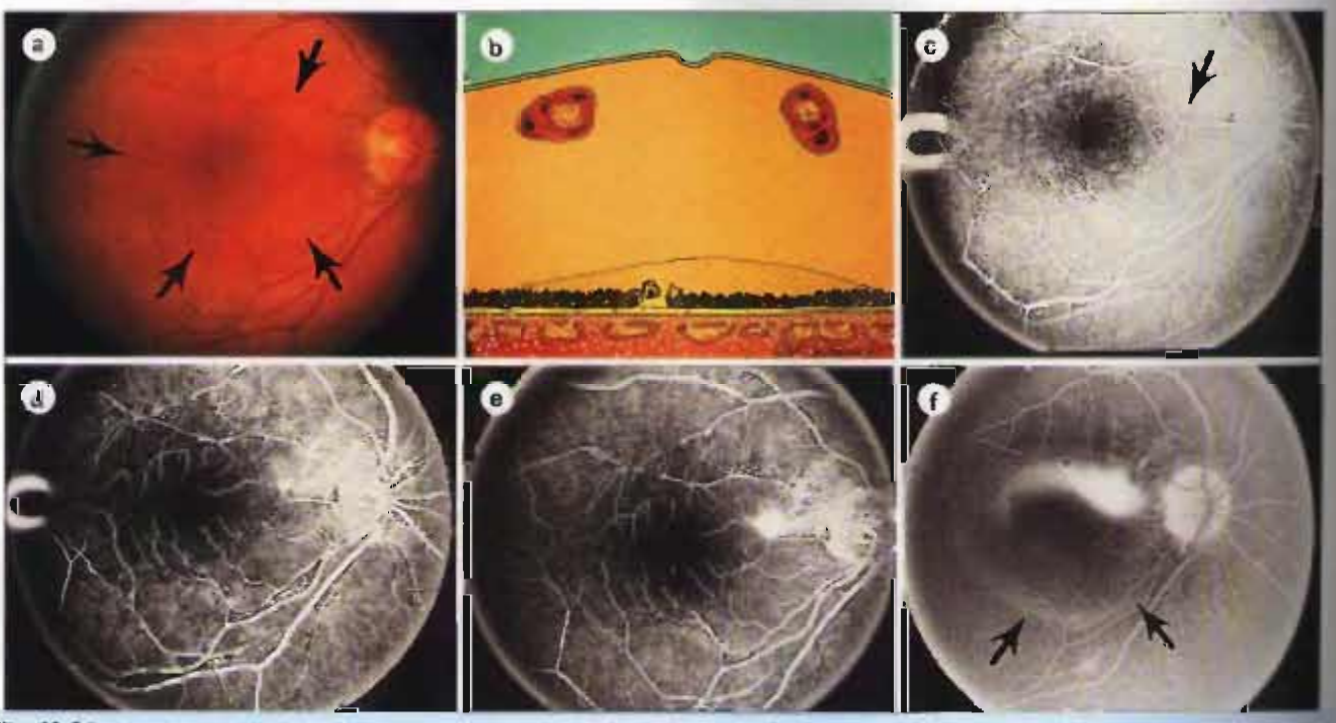


Fig. 13.28
Hyperfluorescence due to pooling of dye in the subretinal space in central serous retinopathy (see text) (Courtesy of Wilmer Institute)

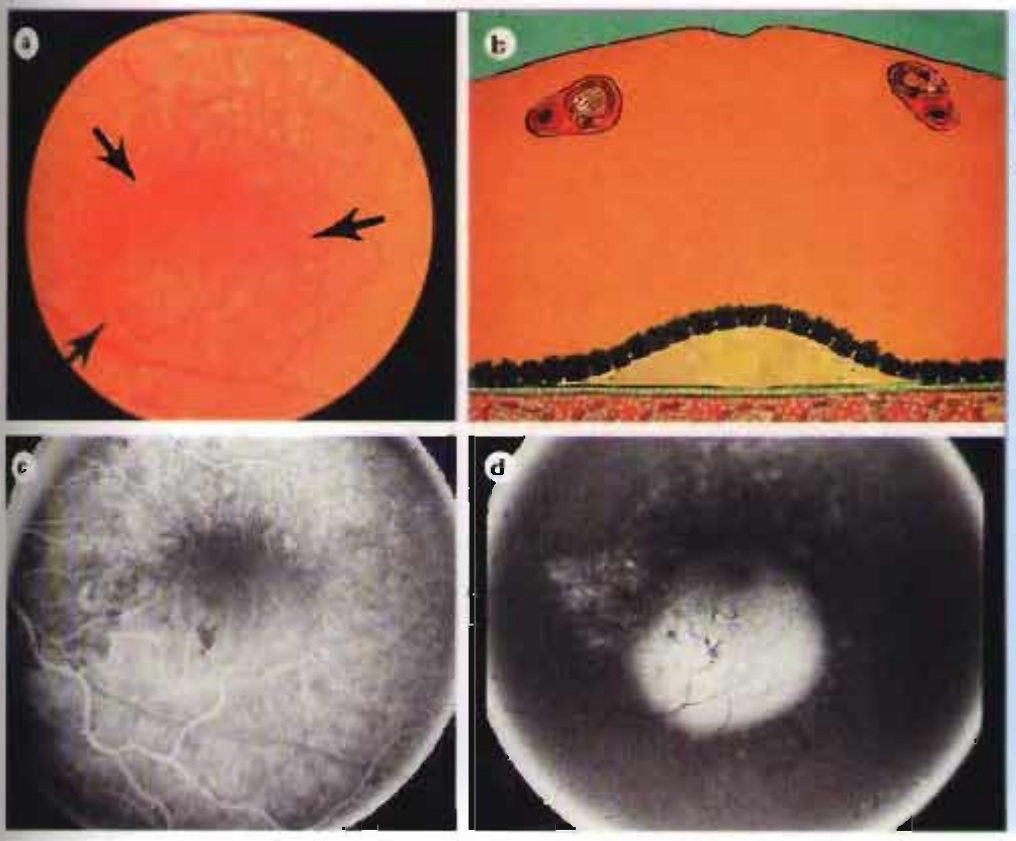


Fig. 13.29
Hyperfluorescence due to pooling of dye in the subpigment epithelial space in PED (see text)
(Courtesy of Wilmer Institute)

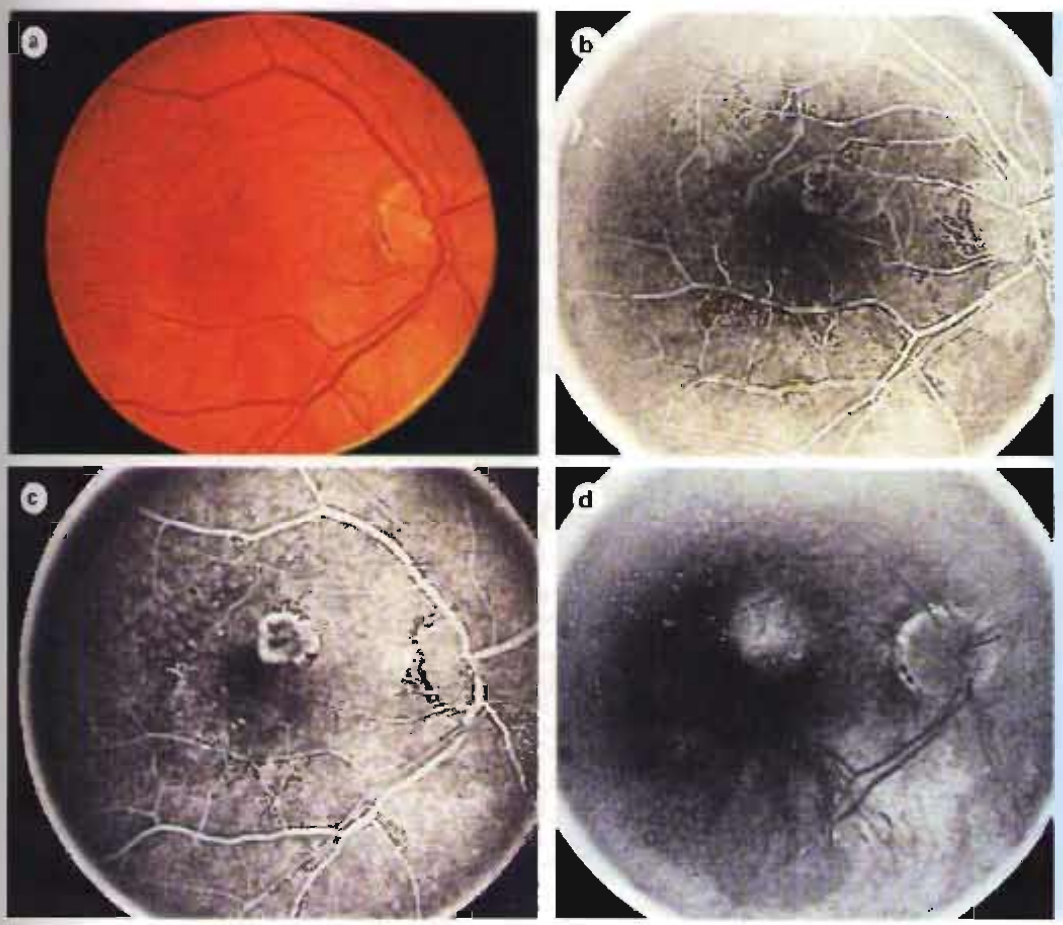


Fig. 13.30
Hyperfluorescence due to leakage from choroidal neovascularization (see text)
(Courtesy of Wilmer Institute)

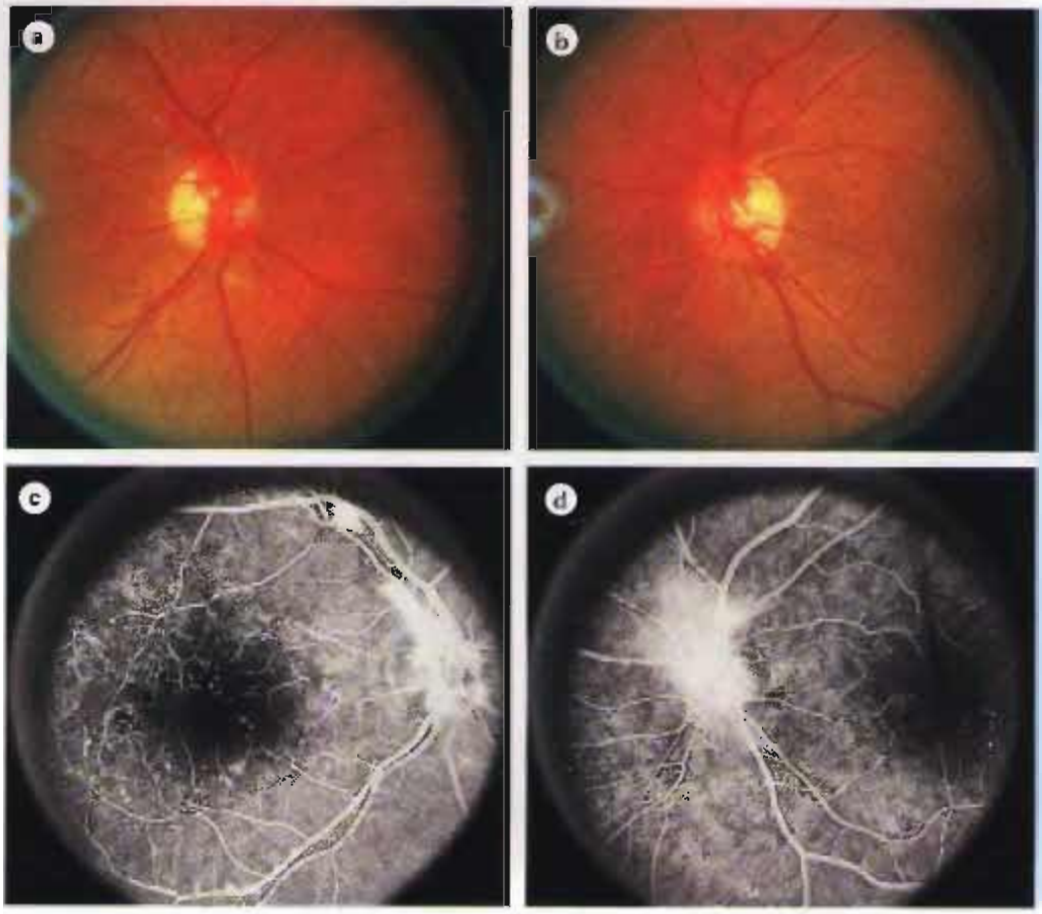


Fig. 13.31
Hyperfluorescence due to leakage from disc new vessels in proliferative diabetic retinopathy (*see text*) (Courtesy of Wilmer Institute)

*b. **Breakdown of the inner blood–retinal barrier***, as in cystoid macular oedema, is characterized by hyperfluorescence beginning in the arteriovenous phase, which increases in size and intensity, giving rise to the characteristic 'flower-petal' pattern seen in the late phase (*see* Fig. 13.13d).

*c. **Abnormal retinal or disc vasculature***, as in proliferative diabetic retinopathy (Fig. 13.31a and b), is characterized by early hyperfluorescence due to rapid filling of the new vessels followed by increasing intense hyperfluorescence due to leakage (Fig. 13.31c and d).

4. **Staining** of tissues as a result of prolonged retention of dye (e.g. drusen) may be seen in the late phase of the angiogram after the dye has left the choroidal and retinal circulations.

Causes of hypofluorescence

Reduction or absence of fluorescence may be due to (a) *blockage* (masking) of a normal quantity of fluorescein in a tissue (Fig. 13.32) or (b) *filling defects* of a tissue with resultant low fluorescein content.

1. **Blockage of retinal fluorescence** may be caused by lesions anterior to the retina. This may involve the large superficial vessels, capillaries or both, depending on the location of the lesion as follows:

*a. **Vitreous opacities*** and ***preretinal lesions*** such as blood (Fig. 13.33a) will block all fluorescence (Fig. 13.33b).

*b. **Deep retinal lesions*** such as intraretinal haemorrhages and hard exudates will block only capillary fluorescence, sparing that from the larger retinal vessels.

2. **Blockage of background choroidal fluorescence** is caused by all conditions that block retinal fluorescence as well as the following which block only choroidal fluorescence:

*a. **Subretinal*** or ***sub-RPE lesions*** such as blood (Fig. 13.34).

*b. **Increased density of the RPE*** such as in congenital hypertrophy of the RPE (Fig. 13.35).

*c. **Choroidal lesions*** such as naevi.

3. **Filling defects** may result from:

*a. **Vascular occlusion*** which prevents access of dye to the tissues. The occlusion may involve the choroidal circulation or the retinal arteries, veins or capillaries (capillary drop-out) (*see* Fig. 14.13).

*b. **Loss of the vascular bed*** which may occur in severe myopic degeneration or choroideremia (*see* Fig. 15.60).

Stepwise approach to reporting angiograms

A fluorescein angiogram should be interpreted systematically to optimize diagnostic accuracy, as follows:

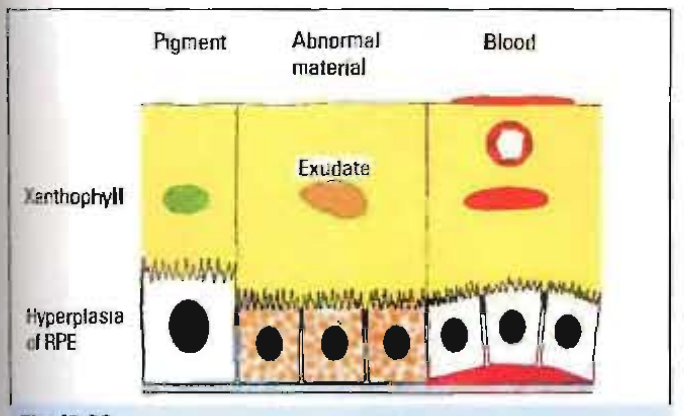


Fig. 13.32
Causes of blocked fluorescence (*see text*)

1. Comment on the red-free photograph.
2. Indicate the phase of the angiogram.
3. Indicate any hyper- or hypofluorescence and any delay in filling.
4. Indicate any characteristic features such as a smoke-stack or lacy filling pattern (*see later*).
5. Indicate any change in the area or intensity of fluorescence.

NB: It is important to take into consideration the patient's history and ophthalmoscopic findings before drawing conclusions from the angiogram.

Indocyanine green angiography

General principles

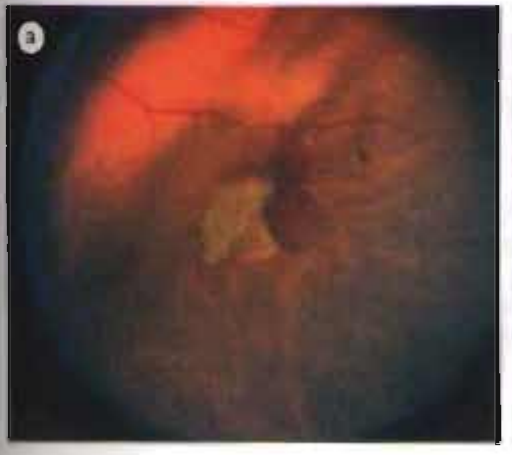
While FA is an excellent method of showing the retinal circulation against the uniform dark background of the RPE, it is not helpful in delineating the choroidal circulation. In contrast, indocyanine green (ICG) angiography is of particular value in studying the choroidal circulation and is a useful adjunct to FA in the investigation of macular disease.

1. **ICG binding**. About 98% of ICG molecules bind with serum proteins (mainly albumin) on entering the circulation. This phenomenon reduces the passage of ICG through the fenestrations of the choriocapillaris, which are impermeable to albumin.
2. **Fluorescence** of ICG is only 1/25 that of fluorescein. The excitation peak is at 805 nm and emission at 835 nm, in the near-infrared spectrum. Infrared light absorbed and emitted by the dye readily penetrates normal ocular pigments such as melanin and xanthophyll, as well as exudates or thin layers of subretinal blood. The filters used are infrared barrier and excitation.

Photographic technique

1. ICG powder is mixed with aqueous solvent to provide 40 mg in 2 ml.

Fig. 13.33
Hypofluorescence due to blockage of all fluorescence by a preretinal haemorrhage (*see text*) (Courtesy of Wilmer Institute)



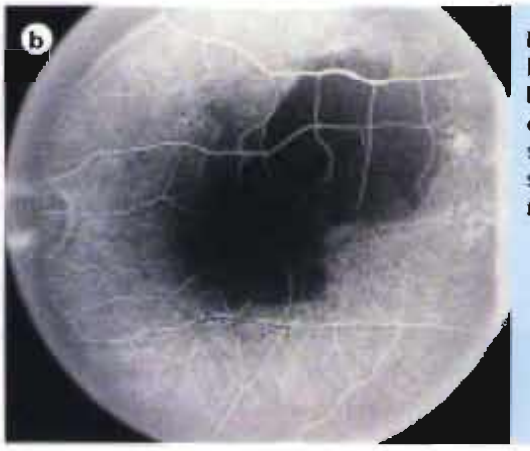


Fig. 13.34
Hypofluorescence due to blockage of background choroidal fluorescence by subretinal pigment epithelial and subretinal haemorrhages (*see text*) (Courtesy of Wilmer Institute)

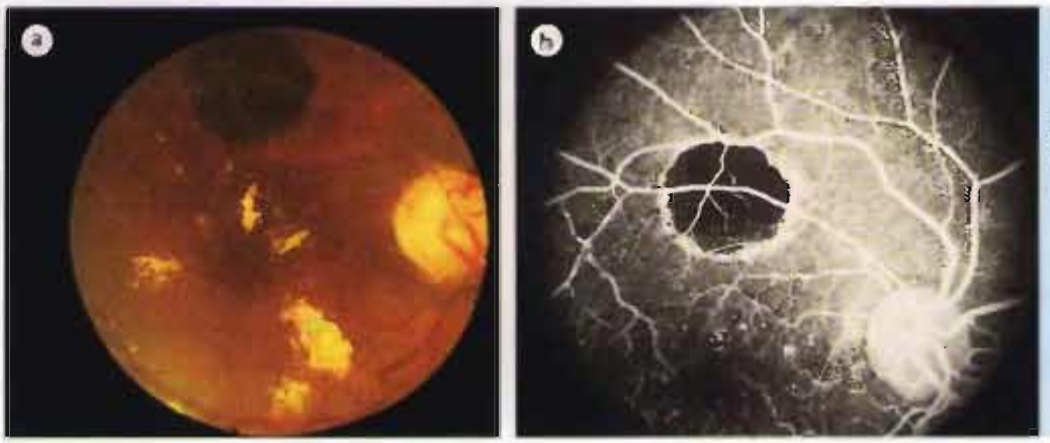


Fig. 13.35
Hypofluorescence due to blockage of background choroidal fluorescence by congenital hypertrophy of the retinal pigment epithelium and hard exudates (see text)
(Courtesy of Wilmer Institute)

2. The patient is seated in front of the camera with one arm outstretched.
3. A 'red-free' photograph is taken.
4. Between 25 and 40 mg of dye is injected intravenously.
5. Rapid serial photographs are taken initially and then subsequent photographs are taken at about 3 minutes, 10 minutes and 30 minutes.
6. Late phases yield the most useful information, because the dye remains in neovascular tissue after leaving the retinal and choroidal circulations.

If necessary, ICG angiography may be performed simultaneously with or sequentially to FA. ICG videoangiography (ICG-VA) is commonly used as a supplementary test to FA in the diagnosis and treatment of occult CNV. The two angiographic systems used in performing ICG-VA are the high-resolution digital fundus camera and the scanning laser ophthalmoscope. ICG-guided laser treatment of occult CNV is based on the detection of focal spots or plaques by the digital ICG-VA. The scanning laser ophthalmoscope is better at detecting the vascular net in the very early transit phase of the ICG-VA.

Adverse effects

These are less common than with FA. Because ICG contains 5% iodine it should not be given to patients allergic to iodine. Its use is also contraindicated in pregnancy. The most common side effects are staining of stool, nausea, vomiting, sneezing and pruritus. Less common manifestations include syncope, skin eruptions, pyrexia, backache and local skin necrosis.

The normal angiogram

1. **Early phase** (2–60 seconds) (Fig. 13.36a)
   - Hypofluorescence of the optic disc associated with poor perfusion of the watershed zone.
   - Prominent filling of choroidal arteries and early filling of choroidal veins.
   - Retinal arteries are visible but not veins.
2. **Early mid phase** (1–3 minutes) (Fig. 13.36b)
   - Filling of the watershed zone.
   - Fading of choroidal arterial filling with more prominent filling of choroidal veins.
   - Both retinal veins and arteries are visible.
3. **Late mid phase** (3–15 minutes) (Fig. 13.36c)
   - Fading of filling of choroidal vessels.
   - Diffuse hyperfluorescence as the result of diffusion of dye from the choriocapillaris.
   - Retinal vessels are still visible.
4. **Late phase** (15–30 minutes) (Fig. 13.36d)
   - Hypofluorescence of choroidal vasculature against a background of hyperfluorescence resulting from staining of extrachoroidal tissue.
   - Lack of visibility of retinal vasculature.
   - The dye may remain in neovascular tissue after it has left the choroidal and retinal circulations.

Causes of abnormal fluorescence

1. **Hyperfluorescence**
   a. *RPE 'window' defect.*
   b. *Leakage* from the retinal or choroidal circulations, or the optic nerve head.
   c. *Abnormal blood vessels.*
2. **Hypofluorescence**
   a. *Blockage of fluorescence* by pigment, blood or exudate
   b. *Obstruction of the circulation.*
   c. *Loss of vascular tissue.*
   d. *RPE detachment* (hyperfluorescent on FA).

Laser photocoagulation

LASER is an acronym for **L**ight **A**mplification by **S**timulated **E**mission of **R**adiation. Retinal laser photocoagulation is essentially a destructive form of therapy dependent on the absorption of light energy by ocular pigments (melanin, haemoglobin and xanthophyll) and its conversion into heat.

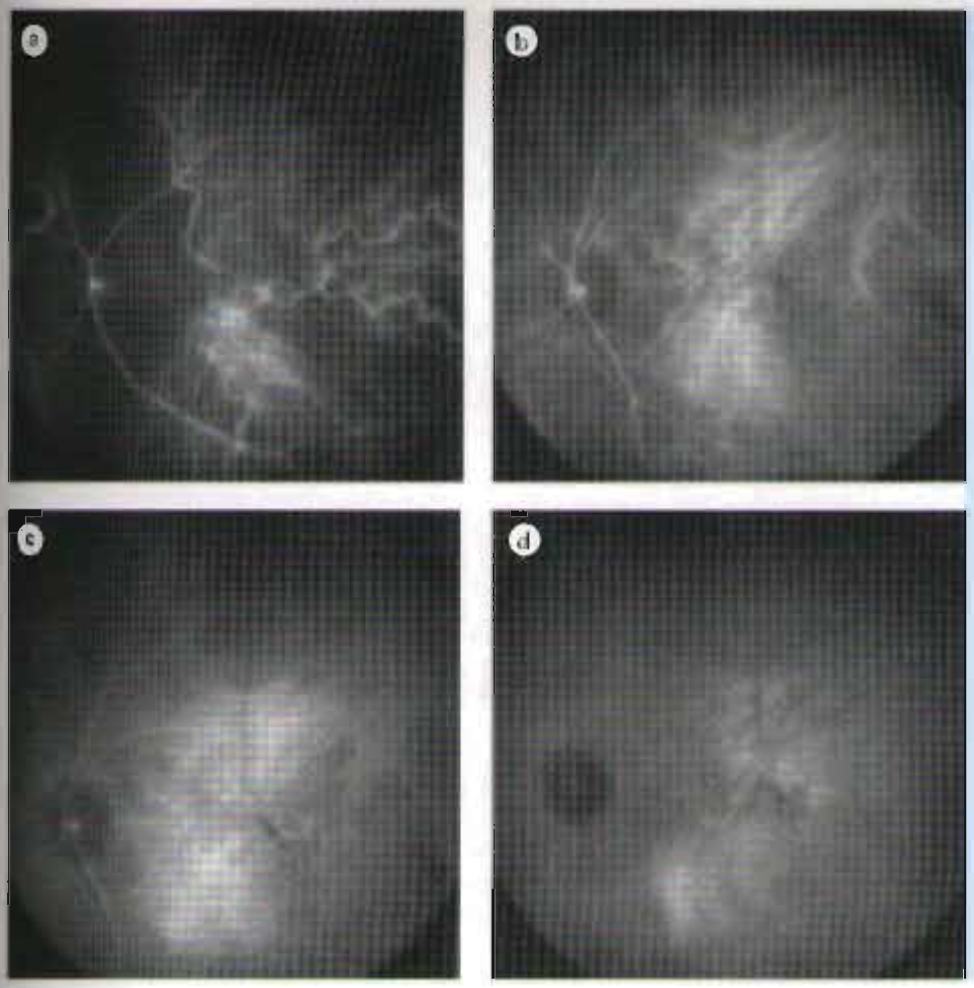


Fig. 13.36
Normal ICG angiogram (see *text*)

Lasers produce a collimated, coherent monochromatic beam that can deliver a large amount of energy to a small area. The purpose of laser therapy is to produce a therapeutic burn to a pre-selected area of the retina while causing minimal damage to surrounding tissue. The main indications for laser photocoagulation are the following:

- Retinal vascular diseases.
- Choroidal neovascular membranes.
- High-risk retinal breaks and predisposing peripheral retinal degenerations.
- Selected intraocular tumours.

Ocular pigments

1. **Melanin** is the most important pigment and is present in the RPE and choroid. Light absorbed by melanin in the RPE is the main source of energy in retinal photocoagulation.
2. **Haemoglobin** best absorbs argon laser energy but is only a significant source of heat when most of the laser energy is concentrated on a blood vessel.
3. **Xanthophyll** is a yellow pigment in the inner retinal layers of the macula. It becomes a heat source only when blue-green argon laser photocoagulation is applied close to the fovea.

Wavelengths

An increasing choice of wavelengths is becoming available, each with its own theoretical advantages and disadvantages. The choice of optimum wavelength depends on the absorption spectrum of target tissue. Currently, the main lasers used for retinal photocoagulation are:

1. **Argon**, which emits coherent blue-green light of 488–515 nm. The beam consists of 70% blue and 30% green light, which can be converted to purely green by the incorporation of a filter. Blue-green wavelengths are well absorbed by all three pigments. However, blue light (488 nm) is undesirable when treating macular disease because it is absorbed by xanthophyll. Green light is absorbed well by melanin and haemoglobin but much less by xanthophyll and is therefore preferred when treatment is required close to the fovea.
2. **Krypton**, which emits yellow light at about 577 nm, is becoming increasingly popular because of its ability to directly coagulate red lesions.
3. **Diode**, which emits infrared light at 780–950 nm.

Practical aspects

1. Delivery systems

a. ***Slit-lamp*** delivery using a special contact lens is the most common method.

b. ***Indirect ophthalmoscope*** with a condensing lens may be used to treat retinopathy of prematurity and other pathology.

c. ***Intraocular*** (endolaser) photocoagulation via fibre-optic probes are used during pars plana vitrectomy.

2. The burn

a. ***Spot size*** is 50–500 μm. The spot size for focal macular treatment is smaller (50–200 μm) than that required for panretinal photocoagulation (300–500 μm). Different contact lenses have variable effects on spot size. For example, while the Goldmann lens does not significantly alter spot size, other contact lens systems and panfundoscopes may enlarge the retinal spot size by 35–50%.

b. ***Power settings*** are 0–3 W (0–3000 mW). Heavily pigmented fundi require less energy than hypopigmented fundi to acquire equivalent burns.

c. ***Exposure times*** are usually 0.01–5 seconds although diode laser photocoagulation (thermotherapy) of certain intraocular tumours requires much longer exposure times.

NB: When spot size is reduced, power remains constant but is spread over a smaller area. The energy level per unit area therefore increases. When changing to a smaller spot size the power must therefore be reduced.

Complications

1. Foveal damage may occur as a result of the following mechanisms:

a. ***Direct burn***, which usually occurs when treating the temporal retinal periphery with the equatorial mirror.

NB: Constant reference to the fovea is essential to avoid this serious complication.

b. ***Oedema*** may occur following extensive (panretinal) photocoagulation. Fortunately it usually resolves spontaneously after a few weeks.

c. ***Pucker*** is also associated with panretinal photocoagulation but its effects on visual acuity are permanent.

d. ***'Spill-over' scarring*** may occur months after initial treatment close to the fovea. In this condition the laser scars gradually increase in size to encroach upon the fovea.

2. Choroidal haemorrhage may occur when a very small (i.e. 50 μm) but high-energy burn ruptures Bruch membrane. This may also lead to CNV (Fig. 13.37c) and subsequent secondary retinal fibrovascular proliferation (Fig. 13.37a, b and d).

3. Contraction of fibrous tissue is a potentially serious complication which may occur when laser burns are applied too closely. Special care should be taken when treating neovascularization associated with large areas of fibrous tissue, because the energy generated may

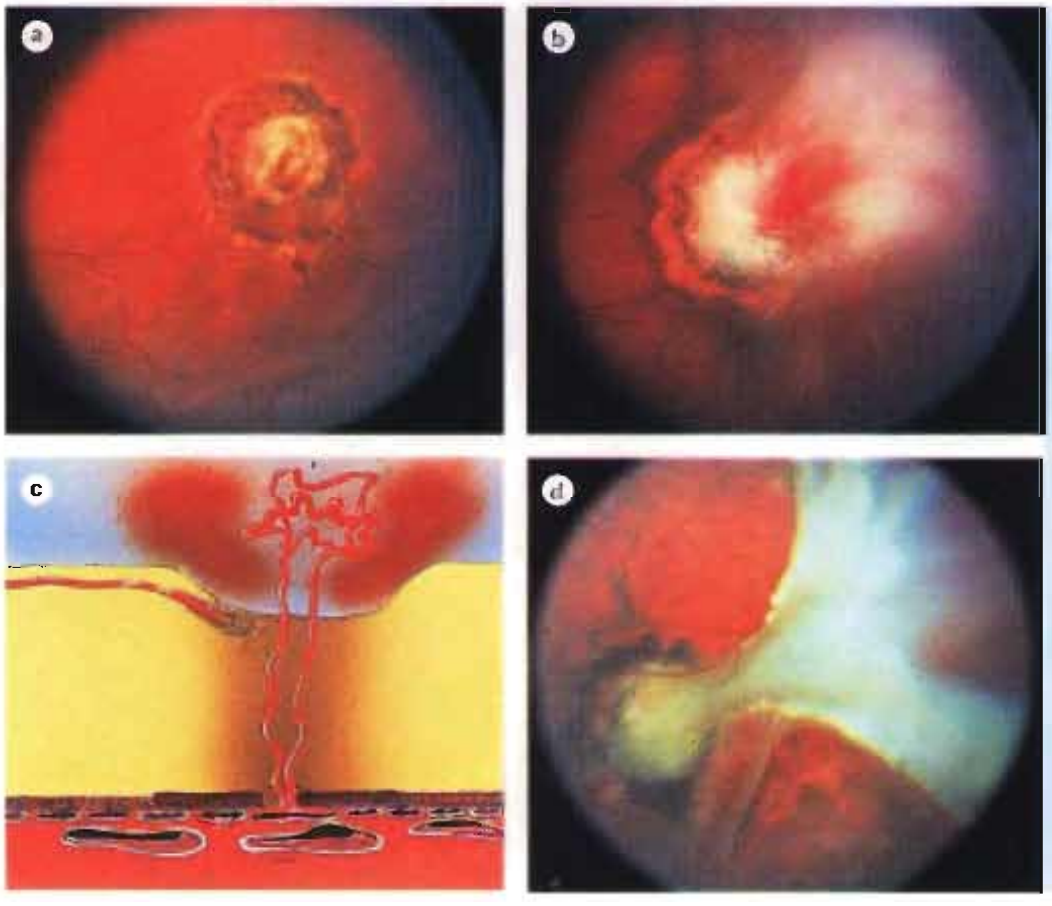


Fig. 13.37
Choroidal neovascularization and secondary fibrous proliferation following inappropriate argon laser photocoagulation (see text)
(Courtesy of Wilmer Institute)

induce contraction and subsequent tractional retinal detachment.

4. **Effects on visual function** from extensive retinal photocoagulation include night blindness, altered colour and light brightness appreciation, and constriction of visual fields.
5. **Other complications**, which are rare, include iris burns, choroidal effusion and vitreous haemorrhage.

Age-related macular degeneration

Introduction

Definition

Age-related macular degeneration (AMD) is a disease of the macular area, most often clinically apparent after 50 years of age, which has early and late characteristics:

1. Early
   - Discrete yellow spots at the macula (drusen).
   - Hyperpigmentation of the RPE.
   - Sharply demarcated areas of RPE depigmentation.
2. Late
   - Geographic atrophy of the RPE with visible underlying choroidal vessels.
   - PED with or without neurosensory detachment.
   - Subretinal or sub-RPE neovascularization.
   - Fibroglial scar tissue, haemorrhage and exudates.

Prevalence

AMD is the most common cause of irreversible visual loss in the western world in individuals over 50 years of age. The prevalence of severe visual loss increases with age. In the USA, at least 10% of individuals between the ages of 65 and 75 years have lost some central vision as a result of AMD. Among those over 75, 30% are affected to some degree. End-stage (blinding) AMD is found in about 1.7% of all individuals aged over 50 years and in about 18% in those over 85 years. AMD may take two patterns:

1. **Atrophic** (dry, non-exudative) AMD, by far the most common, is a slowly progressive disease characterized by drusen and geographic atrophy of the RPE.
2. **Exudative** (wet, neovascular) AMD, less common but devastating, is characterized by CNV and eventual subretinal scarring.

Risk factors

AMD is most prevalent in Caucasians. Genetic and environmental factors appear to modify the risk of visual loss although the relative importance of these is unclear. Cigarette smoking is the only modifiable risk factor.

Drusen

Histopathology

Loss of central vision in AMD is the result of changes that occur in response to deposition of abnormal material in Bruch membrane. This material is derived from the RPE, and its accumulation is thought to result from failure to clear the debris discharged into this region. Drusen consist of discrete deposits of this abnormal material located between the basal lamina of the RPE and the inner collagenous layer of Bruch membrane (Fig. 13.38). The abnormal material also accumulates diffusely throughout Bruch membrane. Thickening of the inner part of Bruch membrane is compounded by excessive production of basement membrane-like material by the RPE. It has been postulated that the lipid content of drusen may be a determinant for subsequent behaviour.

Signs

Drusen appear as yellow excrescences beneath the RPE, distributed symmetrically at both posterior poles. They may vary in number, size, shape, degree of elevation and extent of associated RPE changes. In some patients, drusen may be confined to the region of the fovea, whereas in others the deposits encircle but spare the fovea itself. Drusen are rarely clinically visible before the age of 45 years; they are not uncommon between the ages of 45 and 60 years and almost universal thereafter. With advancing age they increase in size and number.

1. **Hard drusen** are small, round, discrete, yellow-white spots associated with focal dysfunction of the RPE and are usually innocuous (Fig. 13.39).
2. **Soft drusen** are larger, and have indistinct margins (Fig. 13.40). They may slowly enlarge and coalesce to form a solid 'drusenoid' detachment of the RPE (Fig. 13.41a) best demonstrated on FA (Fig. 13.41b). The occurrence of soft coalescent macular drusen is a common precursor of atrophic and exudative AMD. In some cases drusen may undergo secondary dystrophic calcification and acquire a glistening appearance (Fig. 13.42).

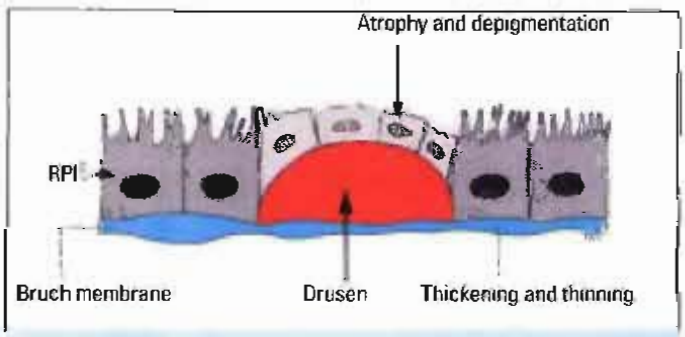


Fig. 13.38
Location of drusen and changes in Bruch membrane

Fluorescein angiography

The findings on FA depend on the state of the overlying RPE and the degree of staining of drusen.

1. **Hyperfluorescence** is caused by both a window defect due to atrophy of the overlying RPE and late staining. It has been postulated that hyperfluorescent drusen are hydrophilic (low lipid content) and predispose to CNV.

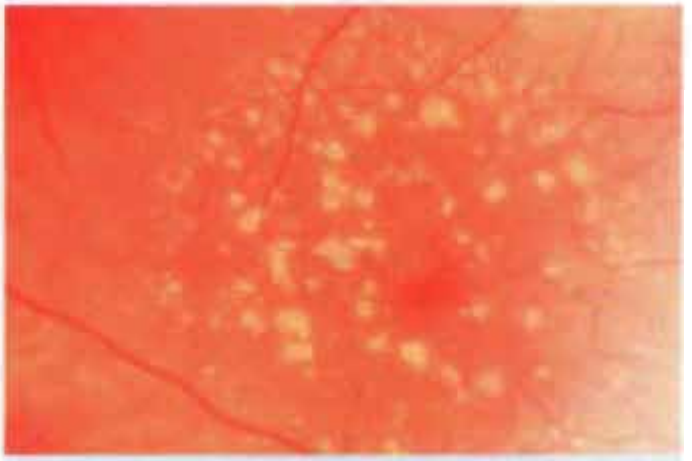


Fig. 13.39
Hard drusen

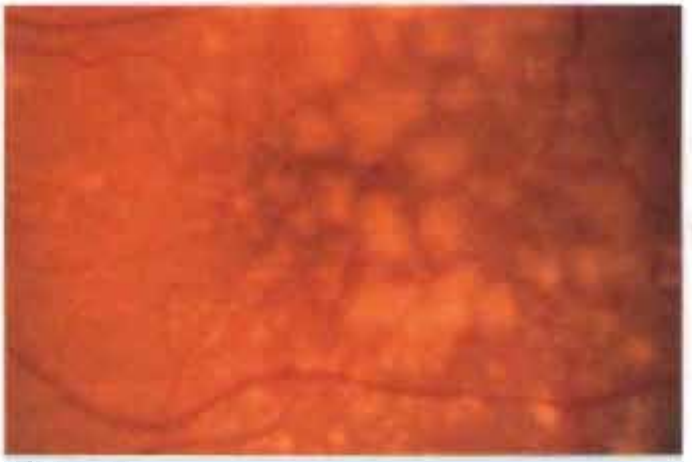


Fig. 13.40
Soft drusen

2. **Hypofluorescent** drusen are hydrophobic (high lipid content) and, if large and confluent, predispose to subsequent detachment of the RPE. A prolonged filling phase of the choroid may indicate diffuse thickening of Bruch membrane.

Differential diagnosis

1. **Familial dominant drusen (Doyne honeycomb dystrophy)** is an uncommon condition in which drusen appear during the second to third decades of life (*see* Chapter 15).
2. **Hard exudates** in diabetic retinopathy may, on cursory examination, be confused with drusen. However, unlike drusen, they lie intraretinally, are arranged in rings or clumps and are associated with vascular changes such as microaneurysms and haemorrhages (*see* Chapter 14).
3. **Type 2 membranoproliferative glomerulonephritis** is a rare disease characterized by haematuria, proteinuria and renal failure. Affected patients manifest bilateral, symmetrical, diffuse yellow, drusen-like lesions at the posterior pole.
4. **Other causes** of retinal flecks include hereditary conditions such as fundus flavimaculatus, Stargardt

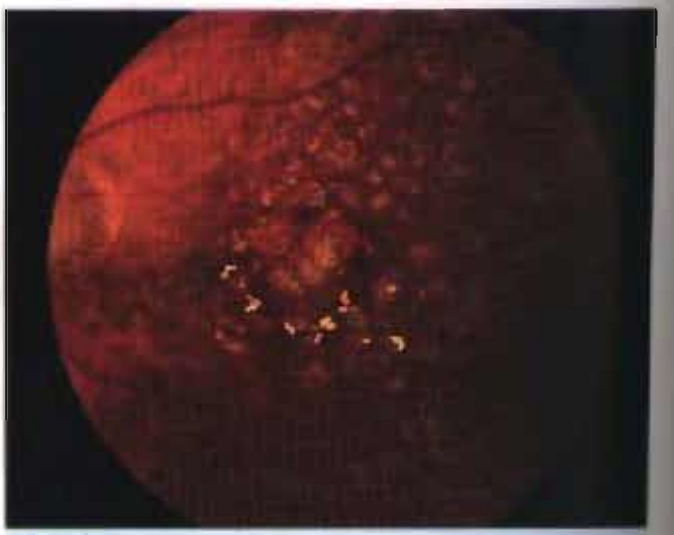


Fig. 13.42
Calcified drusen

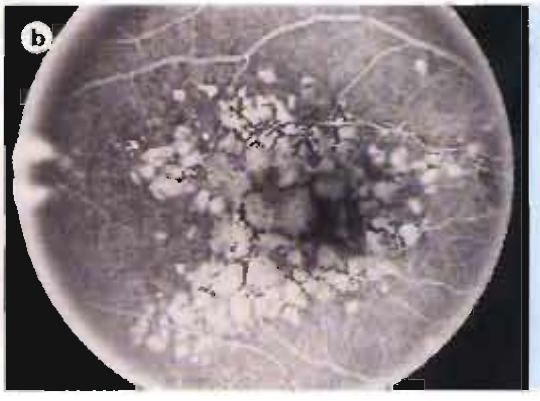


Fig. 13.41
Drusenoid PED (see text)
(Courtesy of Wilmer Institute)

disease, benign flecked retina, North Carolina macular dystrophy and Alport syndrome (*see* Chapter 15). In all of these, the fundus lesions develop at a much earlier age than drusen.

Drusen and AMD

Although many patients with drusen maintain normal vision throughout life, a significant number of elderly patients develop AMD (Fig. 13.43). The exact role of drusen in the pathogenesis of AMD is still unclear, although their chemical composition may be relevant. Features associated with an increased risk of subsequent visual loss include large soft and/or confluent drusen, and focal hyperpigmentation of the RPE, particularly if the other eye has already developed AMD.

Prophylactic treatment

1. **Low-energy argon laser photocoagulation** reduces the number and extent of drusen and may also induce a modest improvement of visual function. Although side effects are uncommon, there is a suggestion that such treatment may predispose to CNV. Prophylactic treatment is therefore currently not recommended.
2. **Supplemental antioxidants** (vitamin C, vitamin E and beta-carotene) and zinc may protect eyes with high-risk drusen from developing AMD.

Atrophic age-related macular degeneration

Atrophic AMD is caused by slowly progressive atrophy of the photoreceptors, RPE and choriocapillaris (Fig. 13.44b and d) although occasionally it may follow subsidence of an RPE detachment (*see* later).

1. **Presentation** is with a gradual impairment of vision over months or years. Both eyes are usually affected but often asymmetrically.

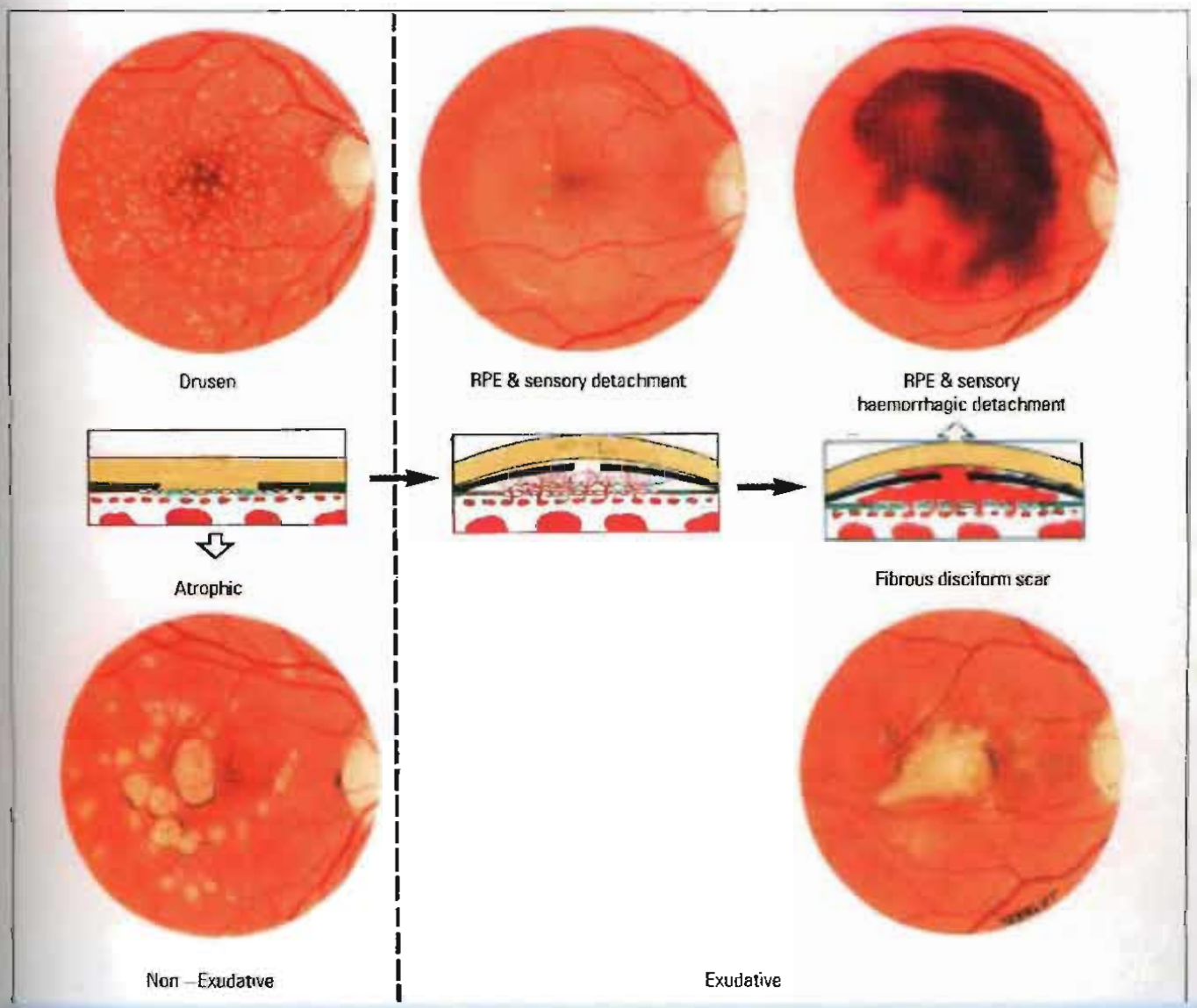


Fig. 13.43
Association between drusen and AMD (*see text*)

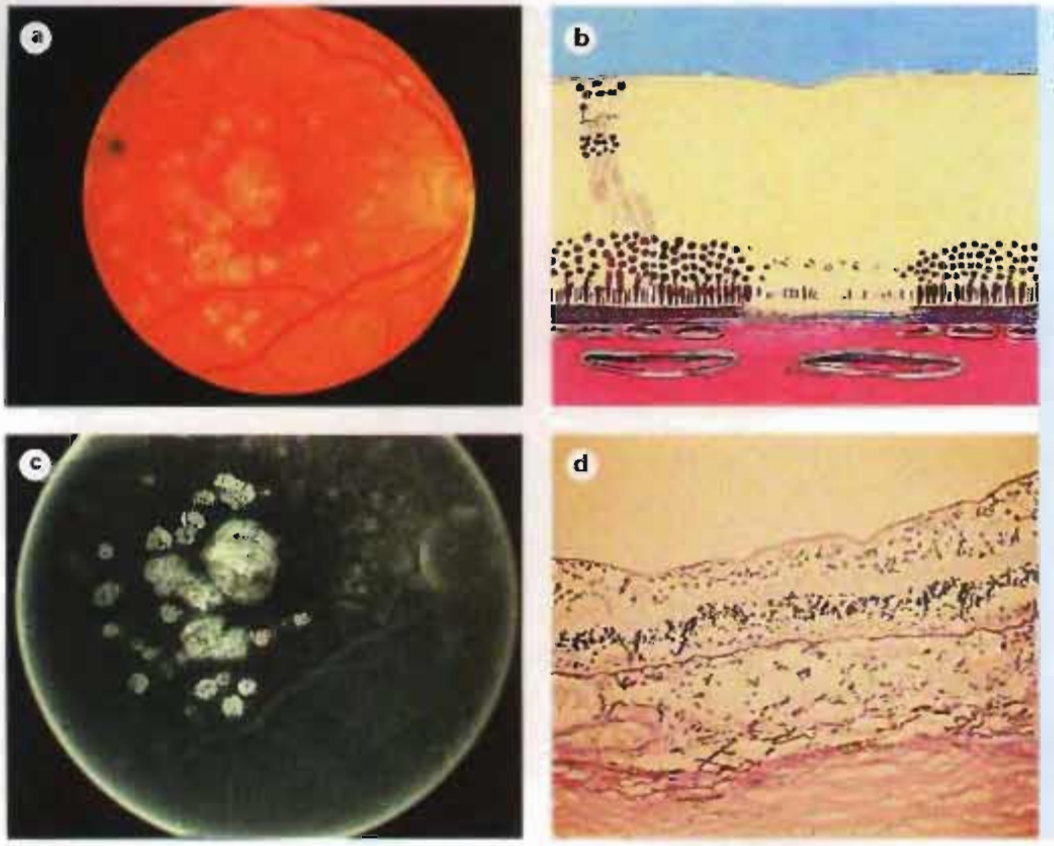


Fig. 13.44
Atrophic AMD (see *text*)
(Courtesy of Wilmer Institute)

2. Signs (in chronological order)
- Focal hyperpigmentation or atrophy of the RPE in association with macular drusen (Fig. 13.45).
- Sharply circumscribed, circular areas of RPE atrophy associated with variable loss of the choriocapillaris (Fig. 13.46).
- Enlargement of the atrophic areas within which the larger choroidal vessels may become visible and pre-existing drusen disappear (geographic atrophy) (Fig. 13.47). Visual acuity is severely impaired if the fovea is involved.

3. FA shows hyperfluorescence due to unmasking of background choroidal fluorescence (*see* Fig. 13.44c) which may be more extensive than that apparent clinically, if the underlying choriocapillaris is still intact.

4. Treatment is not possible although low-vision aids (Fig. 13.48) may be useful in many patients.

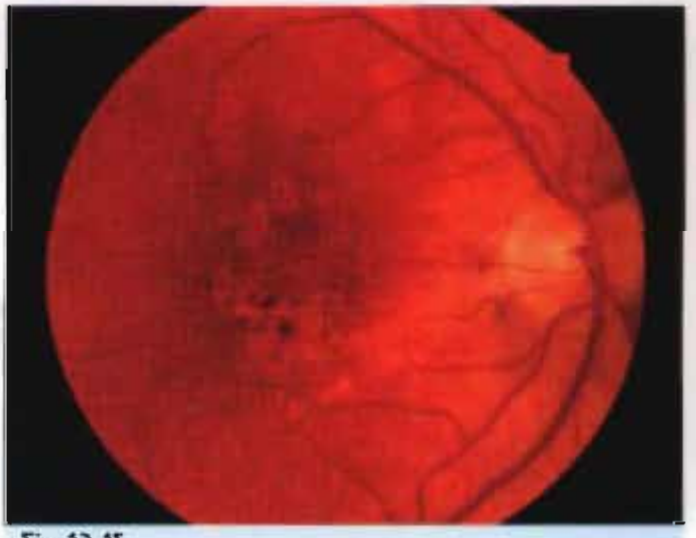
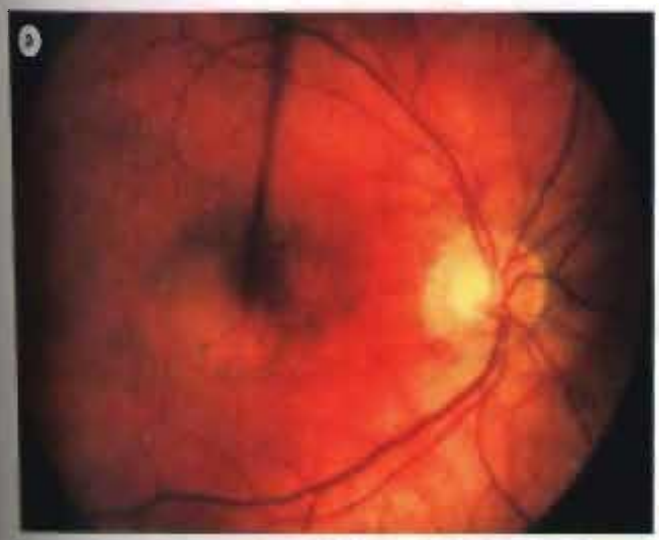


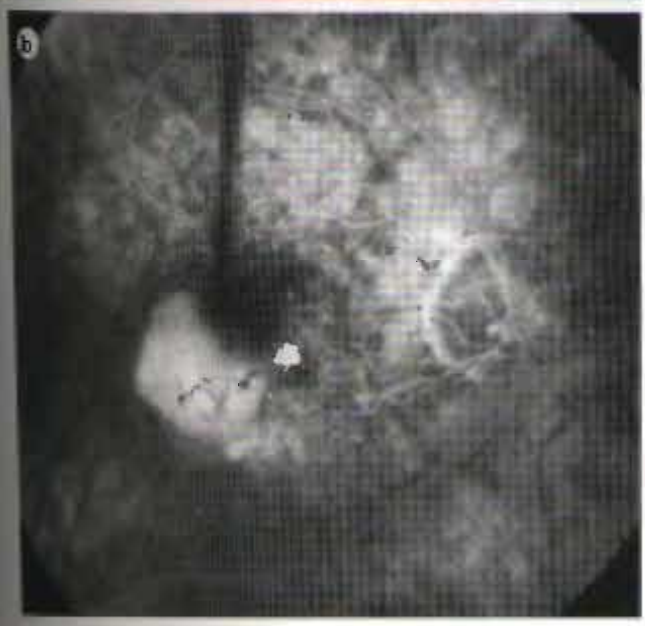
Fig. 13.45
Diffuse RPE changes and drusen in early atrophic AMD

Fig. 13.46
Focal RPE atrophy and drusen in atrophic AMD

Fig. 13.47
Geographic atrophy

Fig. 13.48
Patient trying out a low vision aid





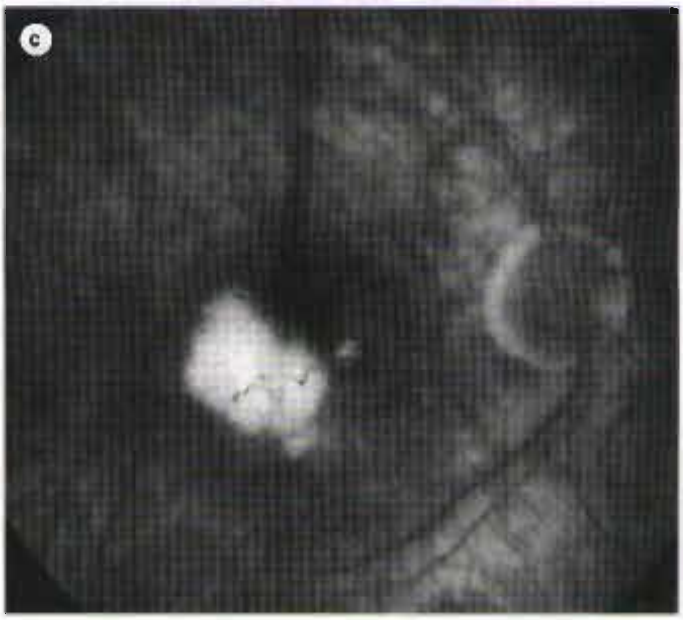


Fig. 13.49
(a) PED; (b and c) FA (see text) (Courtesy of S Milewski)

Retinal pigment epithelial detachment

PED is thought to be caused by reduction of hydraulic conductivity of the thickened Bruch membrane, thus impeding the movement of fluid from the RPE towards the choroid.

Diagnosis

1. **Presentation** is with unilateral metamorphopsia and impairment of central vision.
2. **Signs**
   - Sharply circumscribed, dome-shaped elevation at the posterior pole of varying size (Fig. 13.49a).
   - The sub-RPE fluid is usually clear but may be turbid.
3. **FA**
   - The venous phase demonstrates a well-demarcated area of hyperfluorescence due to pooling of dye under the detachment (Fig. 13.49b).
   - The late phase shows increased hyperfluorescence but no change in size (Fig. 13.49c).
4. **ICG** shows an oval area of hypofluorescence with a faint ring of surrounding hyperfluorescence (Fig. 13.50a and b).

> **NB:** Laser photocoagulation should not be performed for PED.

Course

This is variable and may follow one of the following patterns:

1. **Spontaneous resolution** without residua, particularly in younger patients.
2. **Geographic atrophy** may develop following spontaneous resolution in a minority of patients.
3. **Detachment of the sensory retina** may occur due to breakdown of the outer blood–retinal barrier, allowing passage of fluid into the subretinal space. Because of the relatively loose adhesion between the RPE and sensory retina, the subretinal fluid spreads more widely and is less well defined than in a pure PED.
4. **Occult CNV** may develop or have been present, undetected, from the start (*see* below).
5. **RPE tear formation** (*see* next).

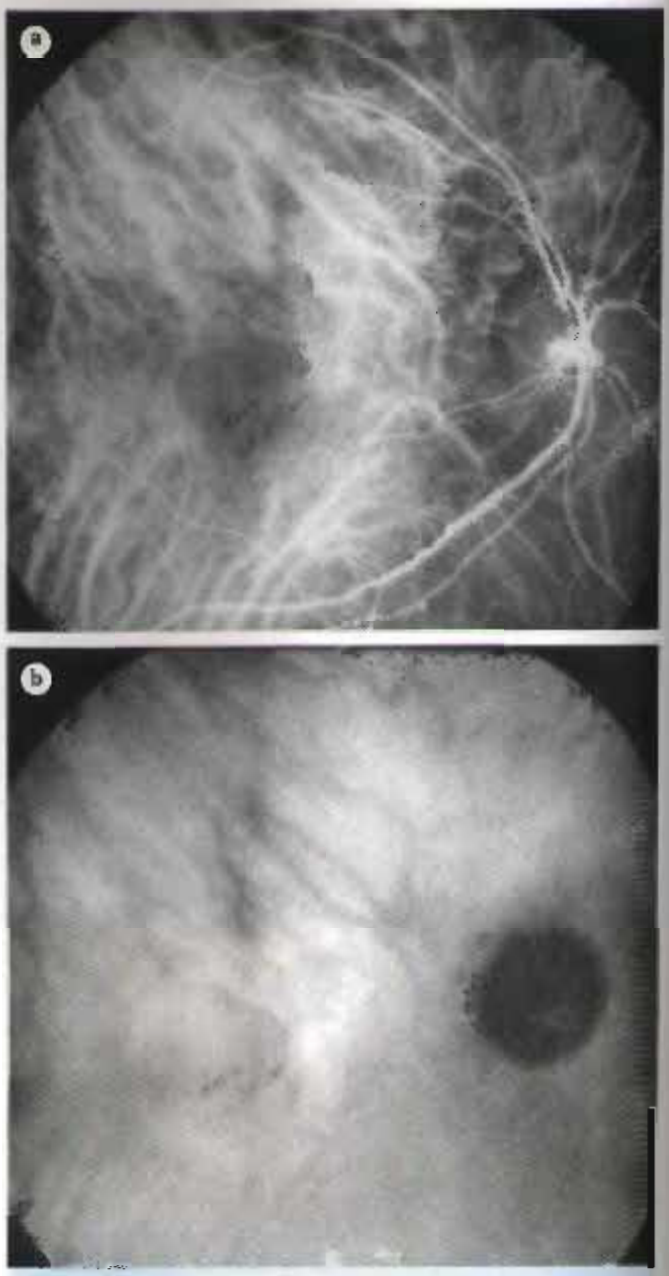
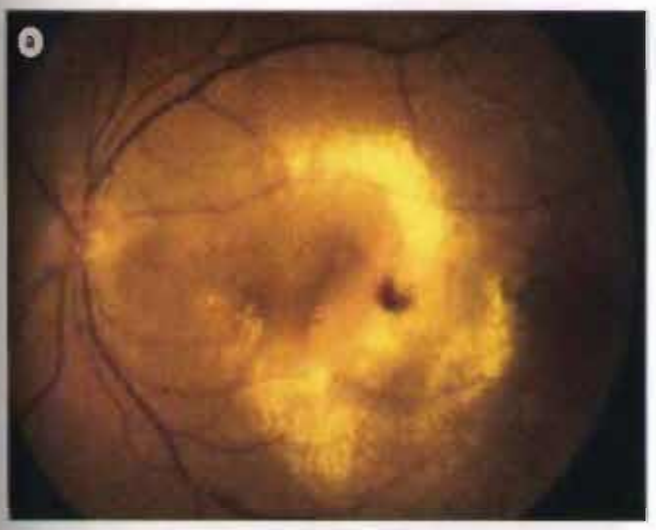


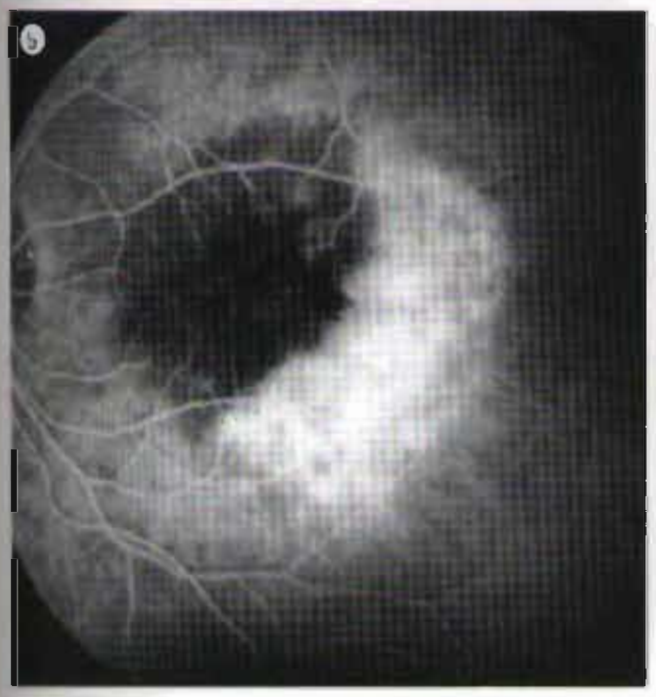
Fig. 13.50
ICG of PED (*see text*) (Courtesy of S. Milewski)

Retinal pigment epithelial tear

A tear of the RPE may occur at the junction of attached and detached RPE if tangential stress becomes sufficient to rupture the detached tissue. Tears may occur spontaneously or following laser photocoagulation of CNV in eyes with PED.

1. **Presentation** is with sudden worsening of central vision.
2. **Signs**. Crescent-shaped RPE dehiscence at the edge of a prior serous detachment with a retracted and folded flap (Fig. 13.51a).
3. **FA** shows hypofluorescence over the flap due to the folded over and thickened RPE, with adjacent hyperfluorescence due to the exposed choriocapillaris (Fig. 13.51b and c).
4. **Prognosis** of subfoveal tears is poor. Detachments of the RPE progressing to tears have an especially poor prognosis and are at particular risk of developing visual loss in the fellow eye. A minority of eyes maintain good visual acuity despite RPE tears, particularly if the fovea is spared.





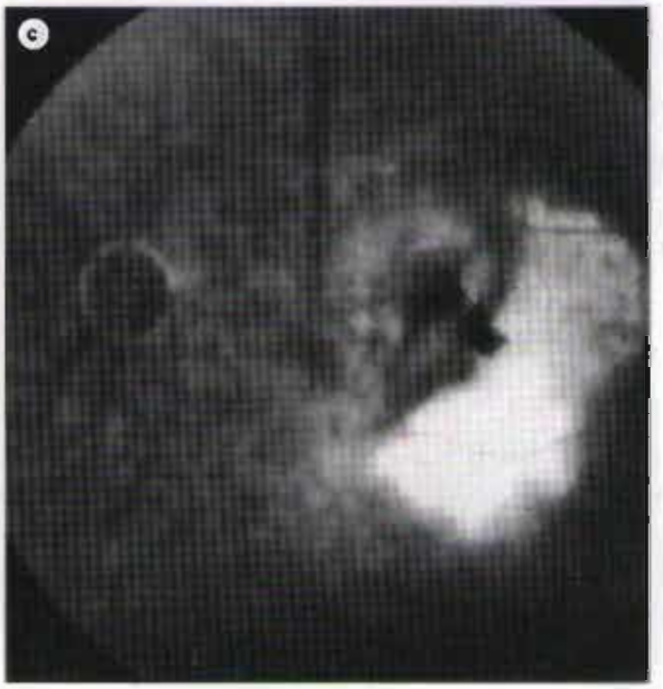


Fig. 13.51
(a) Pigment epithelial rip; (b and c) FA (see *text*) (Courtesy of S. Milewski)

Exudative age-related macular degeneration

Pathogenesis

Exudative AMD is caused by CNV originating from the choriocapillaris which grows through defects in Bruch membrane. CNV may remain confined to the sub-RPE space (type 1) or subsequently extend into the subretinal space (type 2). CNV may precede or follow PED, although these two events are probably not directly related.

Clinical features

1. **Presentation** is with metamorphopsia and blurring of central vision due to leakage of fluid from the CNV. At this stage argon laser treatment may be beneficial.
2. **Signs.** Many membranes cannot be identified ophthalmoscopically.
   - Sub-RPE (type 1) CNV may occasionally be detected clinically as a grey-green or pinkish-yellow, slightly elevated lesion (Fig. 13.52).
   - Subretinal (type 2) CNV may occasionally form a subretinal halo or pigmented plaque.
   - The most frequent signs are caused by leakage from CNV resulting in serous retinal elevation, haemorrhage and subretinal hard exudates (Fig. 13.53).

Fluorescein angiography

FA is important for the detection and precise localization of CNV in relation to the centre of the foveal avascular zone (FAZ).

1. **Classic CNV** is a well-defined membrane which fills with dye in a 'lacy' pattern during the very early phase of dye transit (Fig. 13.54a), fluoresces brightly during peak dye transit (Fig. 13.54b), and then leaks into the subretinal space and around the CNV within 1–2 minutes. The fibrous

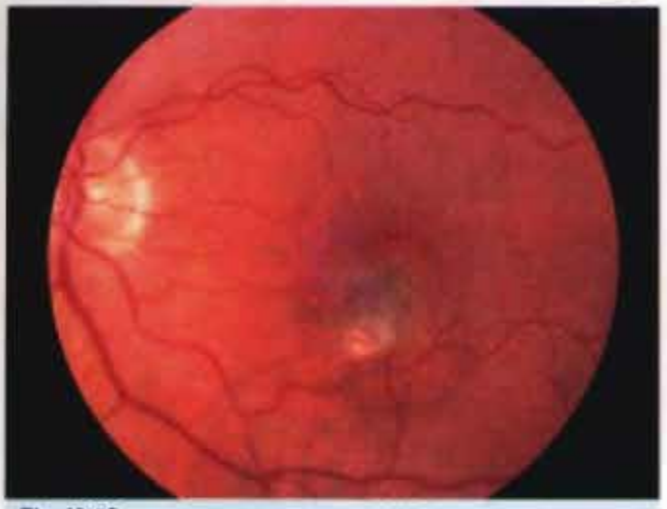


Fig. 13.52
Type 1 CNV below the fovea

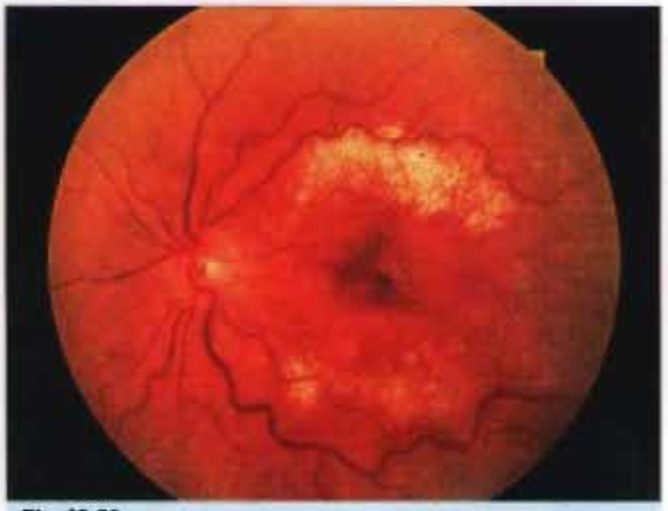


Fig. 13.53
Hard exudates and haemorrhage associated with CNV

tissue within the CNV then stains with dye with late hyperfluorescence (Fig. 13.54c). Classic CNV is classified according to its relation to the centre of FAZ as follows:

a. ***Extrafoveal*** in which the CNV is more than 200 µm from the centre of the FAZ.

b. ***Subfoveal*** in which the centre of the FAZ is involved either by extension from an extrafoveal area or by originating directly under the centre of the fovea. About 70% of CNV extend subfoveally within 1 year. The visual prognosis is very poor.

c. ***Juxtafoveal*** in which the CNV is closer than 200 µm from the centre of the FAZ but does not involve it.

2. **Occult CNV** is a poorly defined membrane which has less precise features on the early frames but gives rise to late leakage.
3. **Fibrovascular PED** is a combination of CNV and PED. The CNV fluoresces more brightly (hot spot) than the detachment (Fig. 13.55a–c). In other cases, the CNV may be obscured by blood (see Fig. 13.57b) or turbid fluid.

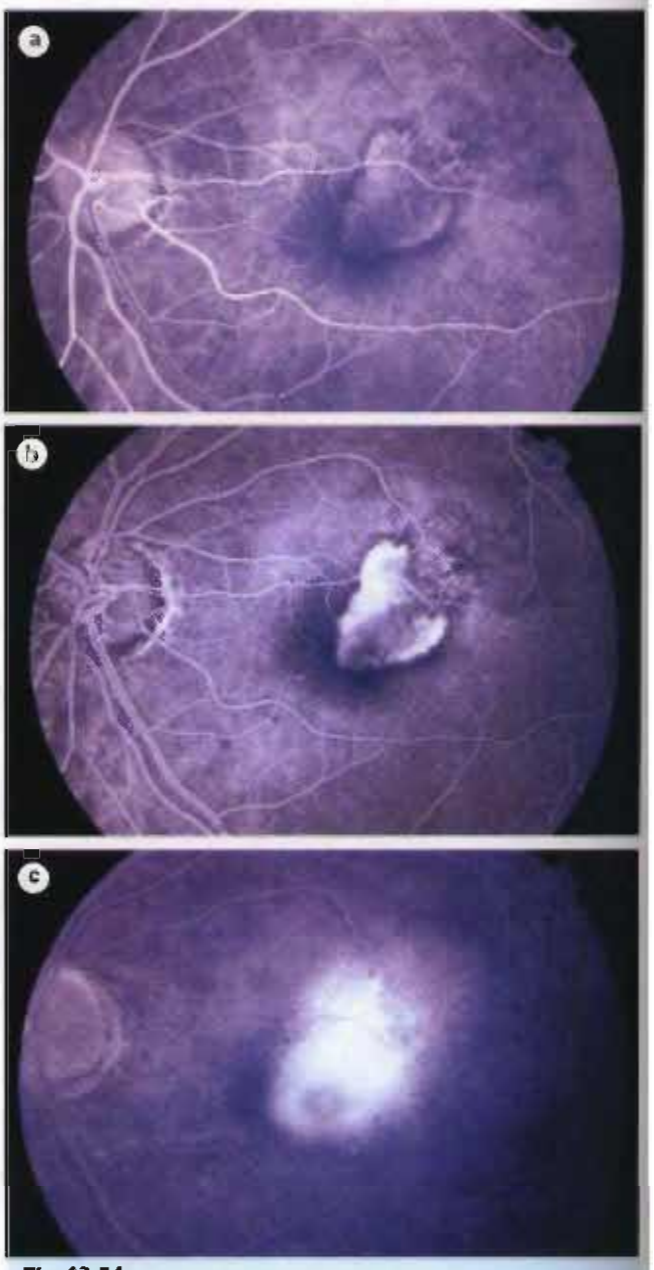


Fig. 13.54
FA of classic CNV (Courtesy of S. Milewski)

Indocyanine green angiography

ICG may be superior to FA under certain circumstances. The longer, near-infrared wavelengths can penetrate the RPE and choroid, and are less absorbed by haemoglobin. These properties allow greater transmission of ICG fluorescence than that of fluorescein and are of particular value in the following circumstances:

- Occult or poorly defined CNV.
- Distinguishing serous from vascularized portions of a fibrovascular PED (Fig. 13.56).
- CNV associated with overlying haemorrhage, pigment or exudate. For example, Fig. 13.57a shows haemorrhage

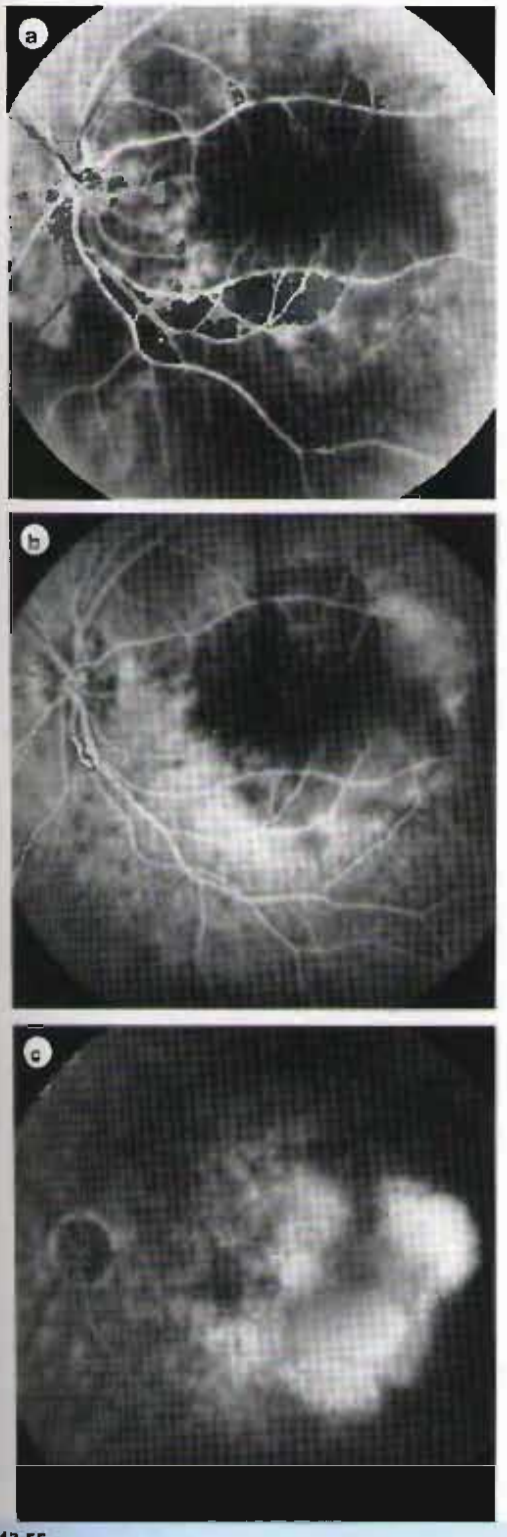


Fig. 13.55
FA of fibrovascular PED. Focal hyperfluorescence superotemporal to the fovea corresponds to juxtafoveal CNV; a larger area of hyperfluorescence lateral to the fovea corresponds to PED (Courtesy of S. Milewski)

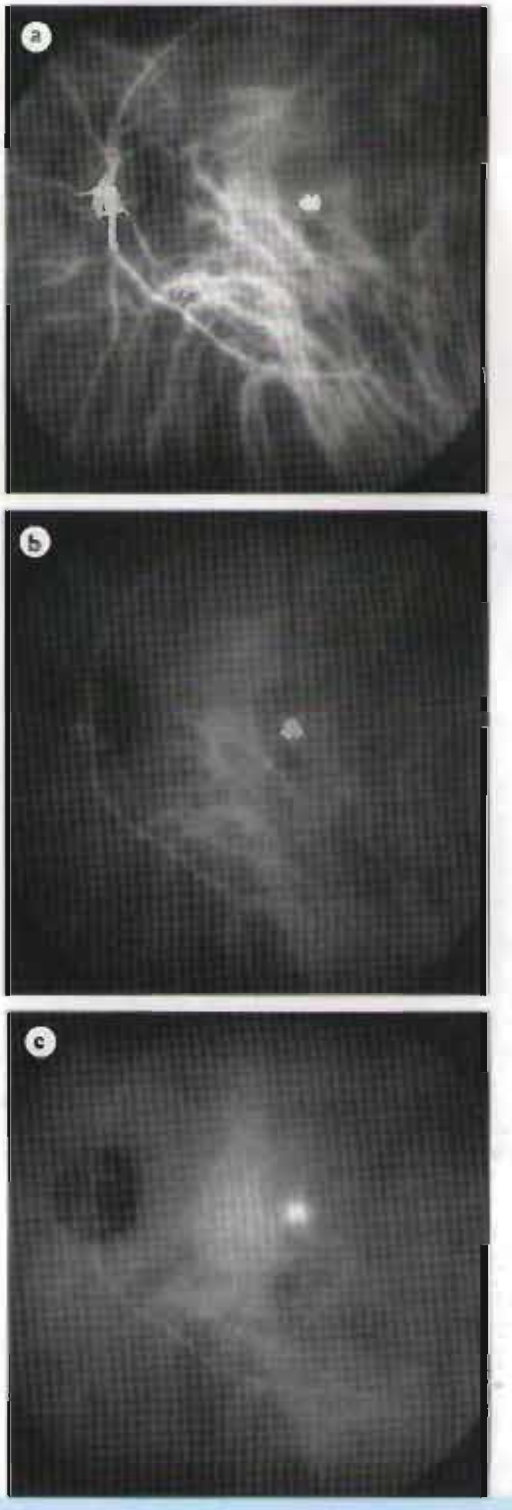


Fig. 13.56
ICG of a fibrovascular PED showing hypofluorescence of the detachment associated with a focal area of hyperfluorescence ('hot spot') corresponding to CNV (Courtesy of S. Milewski)

temporal to the disc and an atrophic macular scar. FA (Fig. 13.57b) shows hypofluorescence corresponding to the haemorrhage but no focal leak suggestive of CNV. ICG, however, shows a 'hot spot' due to CNV under the haemorrhage superotemporal to the disc (Fig. 13.57c).

- Recurrent CNV adjacent to an old photocoagulation scar.

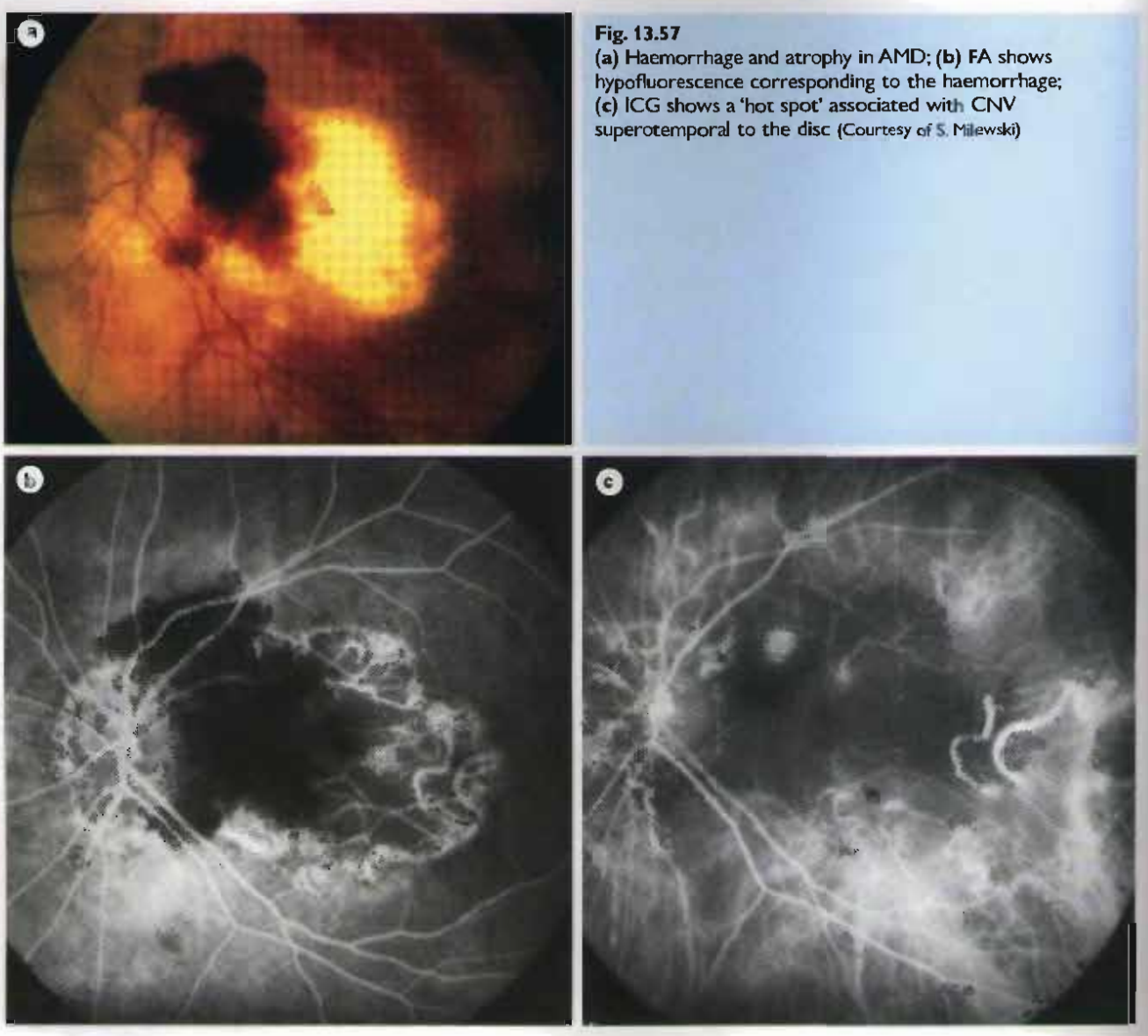


Fig. 13.57
(a) Haemorrhage and atrophy in AMD; (b) FA shows hypofluorescence corresponding to the haemorrhage; (c) ICG shows a 'hot spot' associated with CNV superotemporal to the disc (Courtesy of S. Milewski)

Fig. 13.58
Haemorrhagic pigment epithelial detachment in exudative AMD

Course

The course of untreated CNV is often relentless and the prognosis very poor. The following complications may ensue:

1. **Haemorrhagic PED** caused by rupture of blood vessels within the CNV. Initially, the blood is confined to the sub-RPE space and appears as a dark elevated mound (Fig. 13.58). The haemorrhage may then break into the subretinal space and assume a more diffuse outline and a lighter red colour which may surround or be adjacent to the PED (Fig. 13.59).
2. **Vitreous haemorrhage** may rarely occur when blood under a sensory haemorrhagic detachment breaks through into the vitreous cavity (Fig. 13.60).
3. **Subretinal (disciform) scarring** follows the haemorrhagic episode in which there is gradual organization of the blood, and further ingrowth of new vessels from the choroid (Fig. 13.61). Eventually, a fibrous disciform scar at the fovea causes permanent loss of central vision (Fig. 13.62).

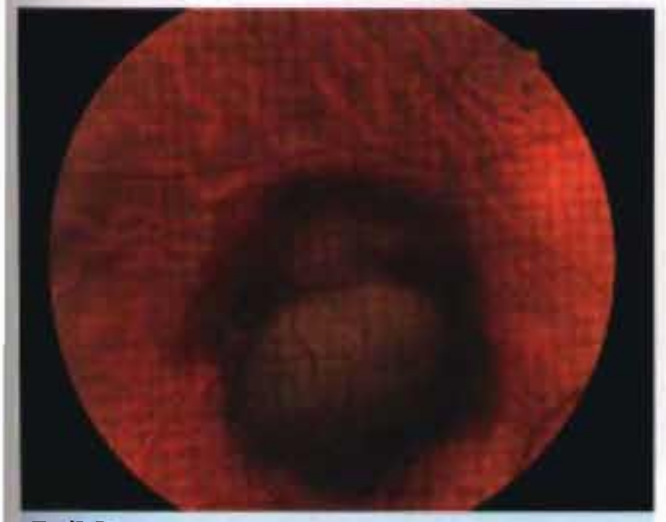


Fig. 13.59
Haemorrhagic pigment epithelial detachment with adjacent subretinal haemorrhage in exudative AMD

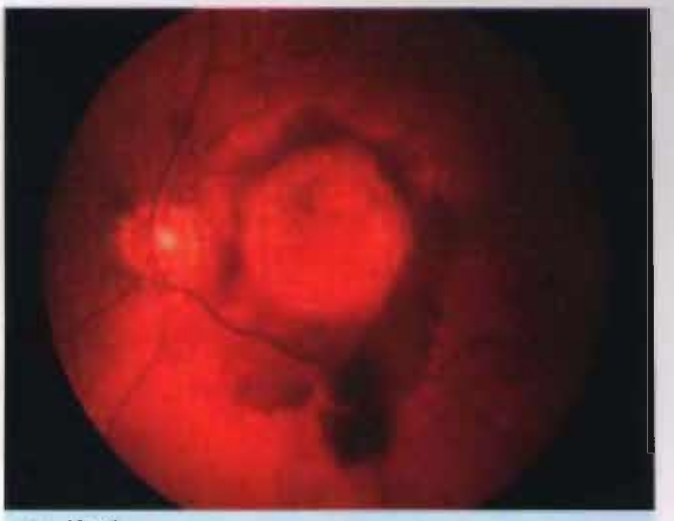


Fig. 13.61
Subretinal scarring surrounded by haemorrhage in exudative AMD

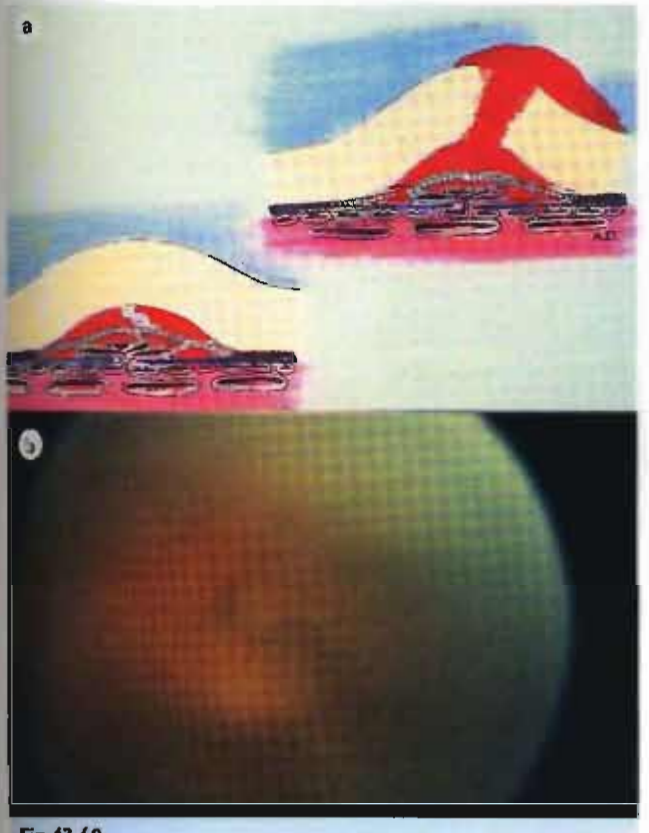


Fig. 13.60
Vitreous haemorrhage in exudative AMD (Courtesy of Wilmer Institute)

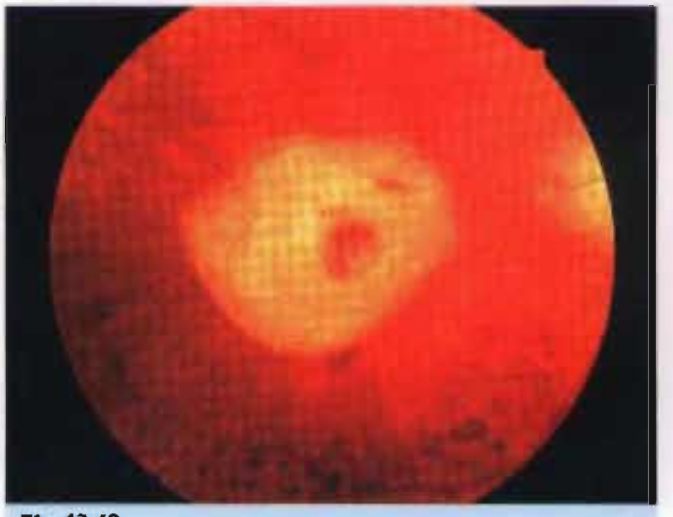


Fig. 13.62
Fibrous disciform scar in exudative AMD

4. **Massive exudation**, both intra- and subretinal, may develop in some eyes with disciform scars as a result of chronic leakage from the CNV (Fig. 13.63). If severe, subretinal fluid may spread beyond the macula and destroy peripheral vision (Fig. 13.64).

Argon laser photocoagulation

Treatment of CNV reduces the risk of severe visual loss in selected cases. The aim is to destroy the CNV, while avoiding damage to the foveola. Because a lesion is more likely to be treatable if detected early, prompt identification with the daily use of the Amsler grid in patients at risk is essential.

1. **Indications.** Extrafoveal or juxtafoveal CNV with well-defined margins (i.e. classic membranes) (Fig. 13.65).
2. **Contraindications**
   a. ***Poorly defined CNV***, because the membrane either is occult or obscured by blood and/or serous RPE detachment. In these cases, treatment, if attempted, is often incomplete because the extent of the CNV cannot be accurately determined.

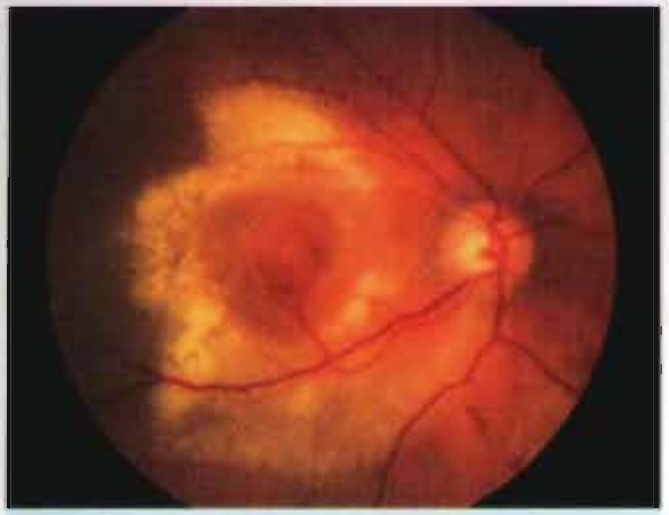


Fig. 13.63
Massive subretinal exudation in exudative AMD

Fig. 13.64
Exudative retinal detachment in exudative AMD

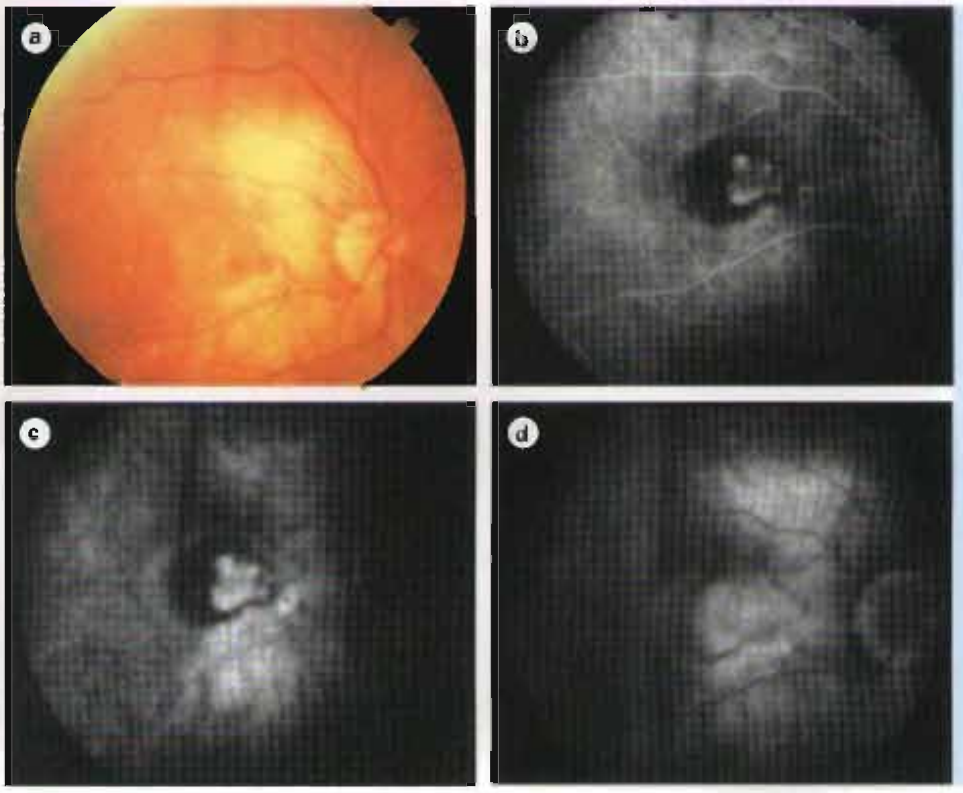


Fig. 13.65
(a) Exudative AMD; (b–d) FA shows classic juxtafoveal CNV

*b. **Poor visual acuity*** (6/36 or less) is often a contraindication because the CNV is likely to be subfoveal. In fact only about 10% of eyes are suitable for treatment at first presentation.

3. Technique

a. Visual acuity is measured for near and distance.
b. The area of the scotoma or visual distortion is documented on the Amsler grid.
c. A good-quality FA, not more than 72 hours old, should be available (*see* Fig. 13.65).
d. Selected frames of the FA are projected onto a screen so that the CNV can be precisely localized in relation to visible retinal landmarks.
e. The perimeter of the lesion is treated with overlapping 200 μm (0.2–0.5 second) burns and then the entire area is covered with high-energy burns. Treatment must extend beyond the margins of the membrane and produce a confluent, intense white burn.
f. A post-treatment fundus photograph is taken to document the extent of treatment.

4. Follow-up should be meticulous so that persistent or recurrent CNV is detected early.

a. Initial follow-up is after 1–2 weeks with an FA to ensure adequacy of treatment (Fig. 13.66).
b. Re-treatment is indicated if there is true persistence or recurrence of CNV more than 200 μm from the centre of the fovea.
c. Because recurrences can occur several years after initially successful treatment, it is important for the patient to continue to self-monitor progress with the regular use of the Amsler grid. On detection of any fresh distortion or scotoma, immediate examination should be arranged.

5. **Results** are frequently disappointing for the following reasons:
   - Using FA as a guide, only a very small proportion of eyes are eligible for treatment.
   - Even after treatment in eligible eyes, the recurrence rate is greater than 50%—most recurrent lesions are subfoveal.

Photodynamic therapy

1. **Principles.** Verteporfin, a photosensitizer or light-activated compound, is injected intravenously. It is then activated locally by illumination with light from a diode laser source at a wavelength (689 nm) that corresponds to an absorption peak of the compound. The main advantage of photodynamic therapy is the ability to selectively damage tissue, attributable to both preferential localization of the photosensitizer to the CNV and irradiation confined to the target tissue. The CNV is irradiated with light levels far lower than those required for thermal destruction by argon laser therapy, enabling treatment of subfoveal CNV.

2. **Indications**
   a. ***Definite*** indications are subfoveal/juxtafoveal, predominantly classic CNV, not larger than 5400 μm in eyes with a visual acuity of 6/60 or better.
   b. ***Possible*** indications are lesions greater than 5400 μm, juxtapapillary CNV with subfoveal extension and CNV from other causes.
3. **Contraindications** are <50% classic CNV and pure occult CNV but these may change in future studies.
4. **Technique**
   - Verteporfin (6 mg/kg body weight) is infused intravenously over 10 minutes.
   - Five minutes later diode laser is applied to the CNV for 83 seconds.
   - Re-treatment is applied to areas of persistent or new leakage at 3-monthly intervals until the entire CNV is obliterated.
5. **Results** in predominantly classic CNV are encouraging with stability or improvement of visual acuity in 60% of cases at 24 months.

Experimental therapies

1. **Surgery**
   a. ***Submacular surgery*** involves the surgical removal of submacular blood, CNV or both. Exact indications and benefits for this type of surgery are currently unknown. Preliminary results suggest a high recurrence rate and the procedure carries a significant risk of complications resulting in visual loss and necessitating further surgical intervention.

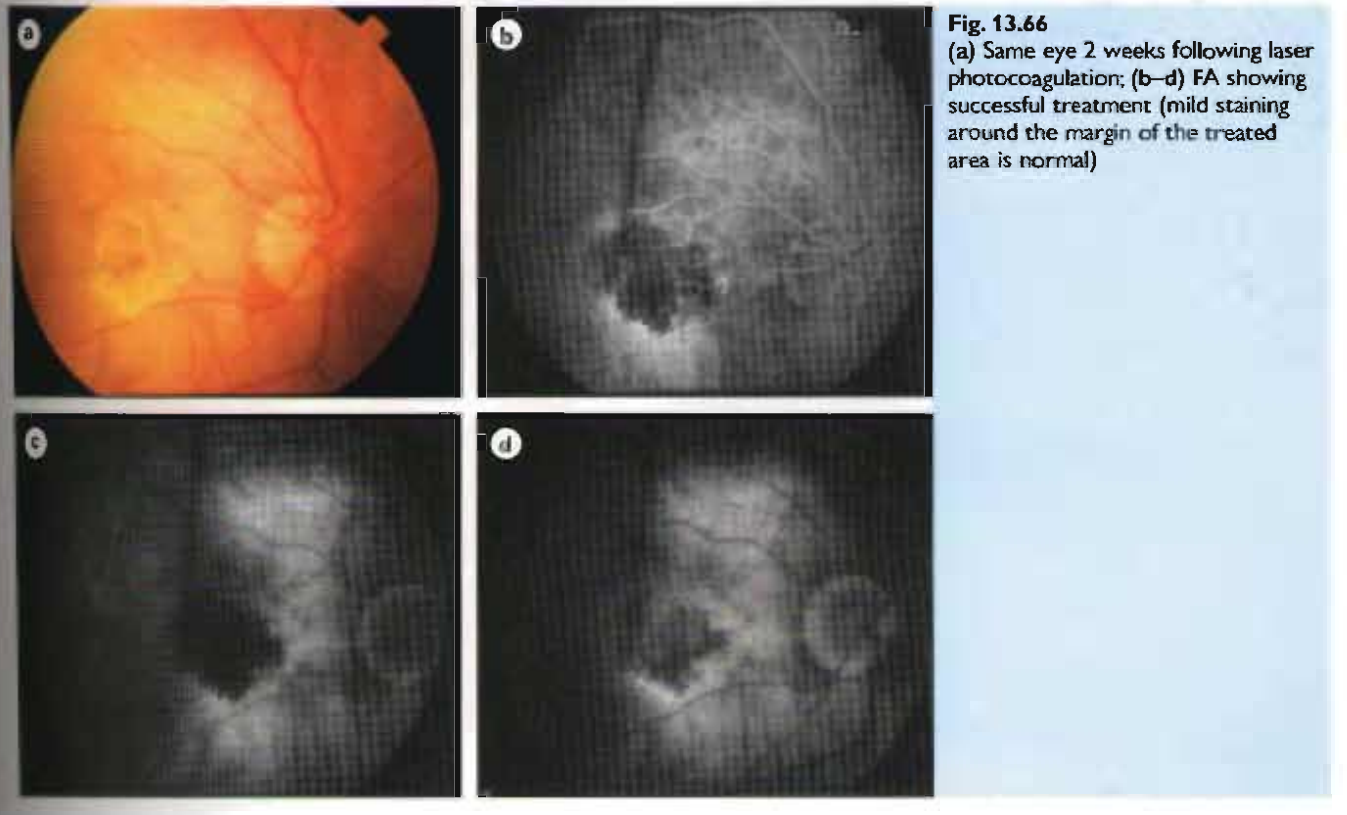


Fig. 13.66
(a) Same eye 2 weeks following laser photocoagulation; (b–d) FA showing successful treatment (mild staining around the margin of the treated area is normal)

*b. **Macular translocation*** is aimed at surgically moving the fovea away from the CNV. The procedure involves chorioscleral folding, vitrectomy and subretinal infusion of balanced salt solution to induce a temporal retinal detachment. Fluid–air exchange is then performed followed by postoperative upright positioning. If appropriate, the CNV may be photocoagulated without the risk of foveal damage. Success is dependent on effective transposition of the fovea away from the diseased CNV complex and the degree of preoperative foveal function. Indications for this modality are still evolving.

*c. **Pneumatic displacement of submacular haemorrhage*** involves injection of gas into the vitreous cavity in order to displace the blood from the fovea. This procedure may also be performed with a fibrinolytic agent called tissue plasminogen activator (tPA).

2. **Transpupillary thermotherapy** with a diode laser (810 nm) may be used for predominantly occult CNV. It has been speculated that this will affect the deeper choroidal vasculature, while sparing the sensory retina. At present there is no data to support this hypothesis.

Age-related macular hole

Age-related (idiopathic) macular holes typically affect elderly females and are caused by progressive tangential vitreoretinal traction at the fovea. Presentation is with severe impairment of central vision, which is often noticed when the fellow eye is closed. In other cases a macular hole first becomes apparent when vision in the fellow eye becomes impaired due to hole formation or other pathology. The diagnosis may also sometimes be made by chance. The risk of involvement of the fellow eye at 5 years is about 15%.

Staging (Fig. 13.67)

1. **Stage 1a** (impending) macular hole is rarely seen clinically and is usually detected in a patient with a full-thickness macular hole (FTMH) in the other eye. It is characterized by a yellow spot at the foveola (Fig. 13.68), which represents an intraretinal cyst which can be confirmed on ocular coherence tomography (*see* Fig. 13.72).
2. **Stage 1b** (occult) macular hole results from centrifugal displacement of the foveolar retina and xanthophyll. It is characterized by a yellow ring with a bridging interface of vitreous cortex. These findings may be associated with recent mild decrease in visual acuity or metamorphopsia. About 50% of stage 1 holes resolve following spontaneous vitreofoveolar separation.
3. **Stage 2** (early FTMH) is characterized by an eccentric, oval, crescentic or horseshoe-shaped retinal defect less than 400 μm in diameter with or without an overlying prefoveal opacity (pseudo-operculum) (*see* Fig. 13.73). True opercula are rare and the pseudo-operculum is formed by the contracted prefoveolar cortical vitreous. Progression from stage 1 to stage 2 takes between 1 week and several months.
4. **Stage 3** (established FTMH) is characterized by a round retinal defect greater than 400 μm in diameter with an attached posterior vitreous face with or without an overlying pseudo-operculum (*see* Fig. 13.74).
5. **Stage 4** is characterized by enlargement of the round defect which is now surrounded by a cuff of subretinal fluid (*see* Fig. 13.75) and exhibits tiny yellowish deposits at the base of the crater (Fig. 13.69). The posterior vitreous is completely detached, often evidenced by a Weiss ring (*see* Fig. 12.20). Visual acuity is decreased primarily due to the absence of photoreceptors within the central defect with a resultant absolute central scotoma. In addition, the surrounding cuff of subretinal fluid and secondary retinal elevation cause a relative scotoma surrounding the absolute central scotoma. Visual acuity tends to deteriorate progressively, stabilizing at 6/60 or worse as the hole reaches its maximal diameter. Some patients may achieve better acuity by employing eccentric fixation.

NB: An FTMH may rarely spontaneously resolve and visual acuity improve.

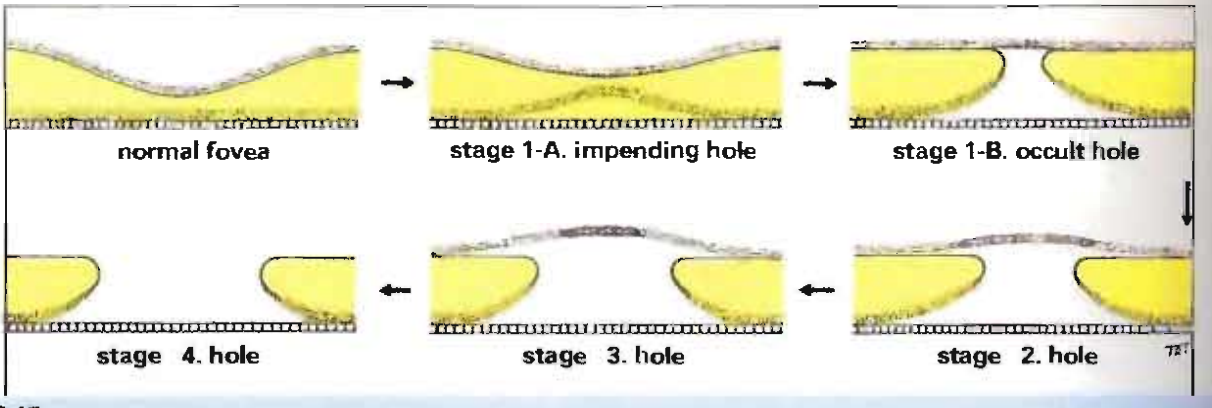
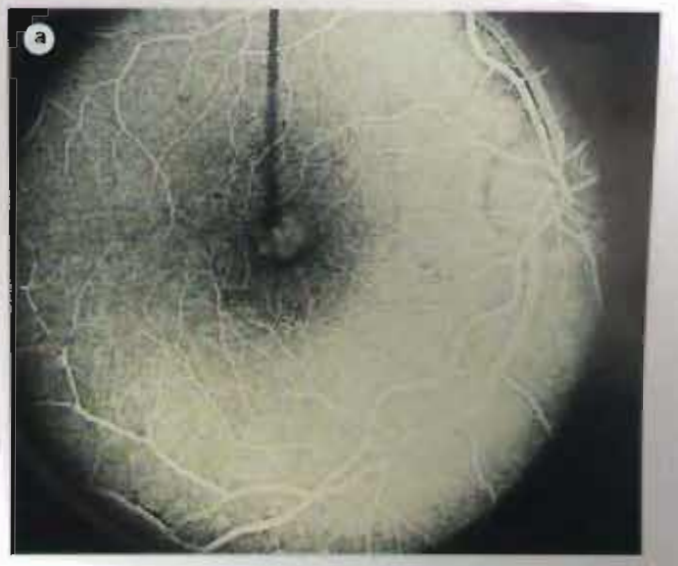


Fig. 13.67
Stages of age-related macular hole (see text)

Fig. 13.68
Stage 1a macular hole



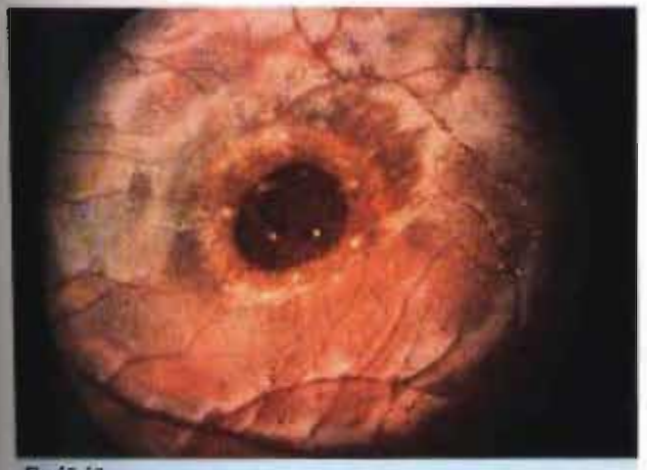


Fig. 13.69
Full-thickness macular hole

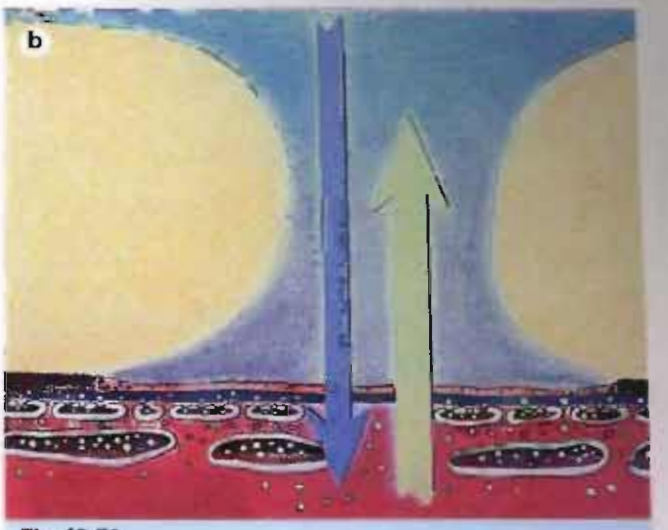


Fig. 13.70
FA of full-thickness macular hole (see text) (Courtesy of Wilmer Institute)

Diagnostic tests

1. **Watzke–Allen** test is performed by projecting a narrow slit beam over the centre of the hole both vertically and horizontally with a 90 D or 78 D lens. A patient with a macular hole will report that the beam is broken or thinned.
2. **Laser aiming beam test** is performed by projecting a 50 μm spot of a laser aiming beam (e.g. He-Ne) at the centre of the hole. A patient with a macular hole will report that the spot has disappeared.
3. **FA** shows a corresponding area of hyperfluorescence (Fig. 13.70a) resulting from unmasking of background choroidal fluorescence caused by a window defect in xanthophyll due to centrifugal displacement (Fig. 13.70b).
4. **Optical coherence tomography** (OCT) provides high resolution optical sections of the retina and affords measurement of retinal thickness. It is useful in the diagnosis and staging of macular holes. It can even measure the volume of a full-thickness macular hole.

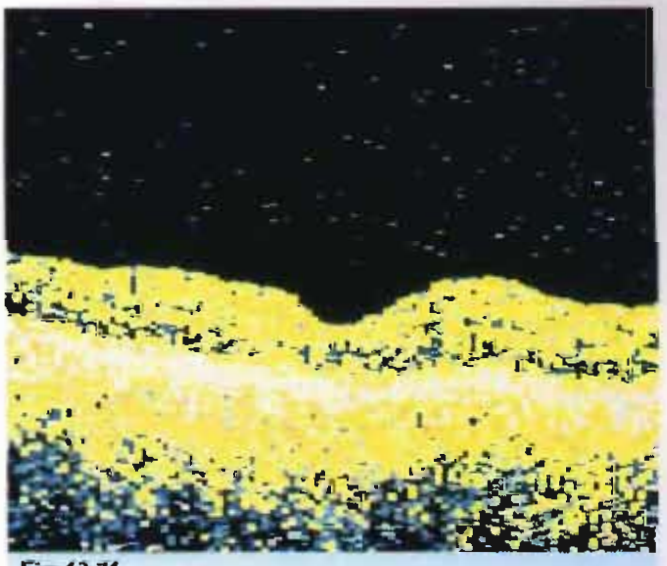


Fig. 13.71
OCT of normal fovea (Courtesy of R. Spaide)

Figure 13.71 shows a normal fovea. Figure 13.72 a stage 1a hole (intrafoveal cyst). Figure 13.73 shows a stage 2 hole with an overlying pseudo-operculum. Figure 13.74 shows a full-thickness stage 3 hole and Figure 13.75 shows a stage 4 hole with a cuff of surrounding subretinal fluid.

Surgical treatment

1. **Indications** are FTMH up to stage 3, associated with a visual acuity worse than 6/18 and a duration less than 1 year.
2. **Technique**
   a. ***Conventional vitrectomy*** consists of removal of the cortical vitreous, internal limiting membrane and gas–fluid exchange followed by strict postoperative face-down positioning. It has been postulated that hole closure is the result of centripetal movement of previously displaced paracentral photoreceptors and not simply re-approximation of the retinal edges to the RPE.
   b. ***'Chemical vitrectomy'*** is a new and less complicated method of treating stage 3 macular holes. An enzyme (plasmin) is injected into the vitreous to chemically detach the vitreous from the retina, without manipulation of the posterior hyaloid. The vitreous is also lavaged with an infusion pipe and vitreous cutter and then 70–80% of the vitreous cavity is filled with 16% C_3F_8. Postoperatively the patient is positioned face-down.
3. **Results**. Following successful surgery, visual improvement is achieved in 80% of eyes, with a final visual acuity of 6/12 or better in up to 65%. Figure 13.76a shows an FTMH and Figure 13.76b the postoperative appearance following successful surgery.
4. **Complications** are those associated with vitrectomy, such as retinal detachment and acceleration of cataract. Permanent visual field defects, often inferotemporal, may develop.

Differential diagnosis

1. **Other macular holes**
   a. ***High myopia***, if associated with posterior staphyloma, may be associated with macular hole formation which can lead to retinal detachment. The subretinal fluid is confined to the posterior pole and seldom spreads to the equator.

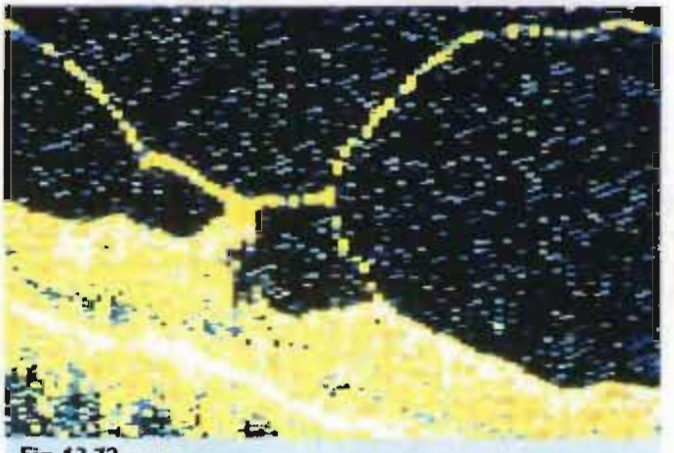


Fig. 13.72
OCT of stage 1a macular hole (Courtesy of R. Spaide)

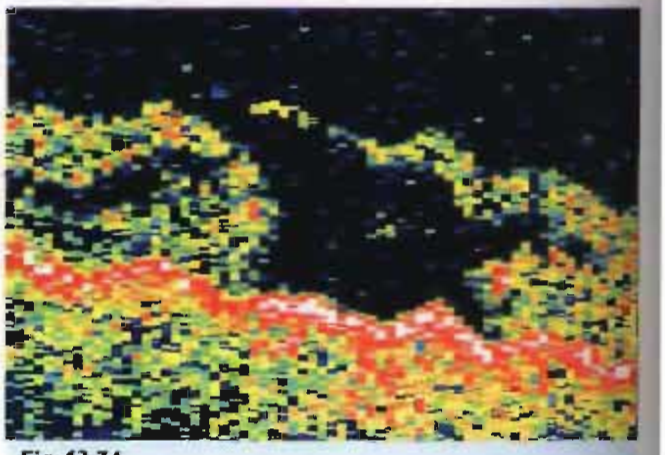


Fig. 13.74
OCT of stage 3 macular hole (Courtesy of V. Tanner)

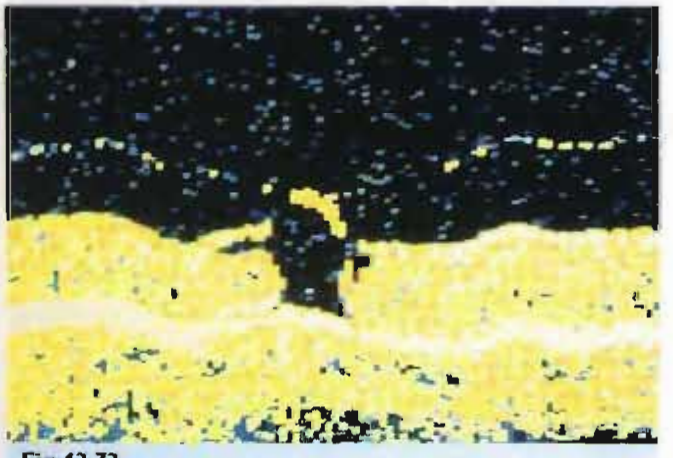


Fig. 13.73
OCT of stage 2 macular hole (Courtesy of R. Spaide)

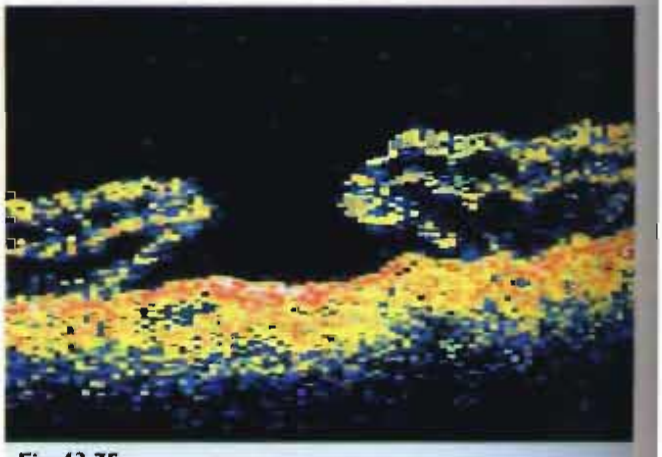


Fig. 13.75
OCT of stage 4 macular hole (Courtesy of V. Tanner)

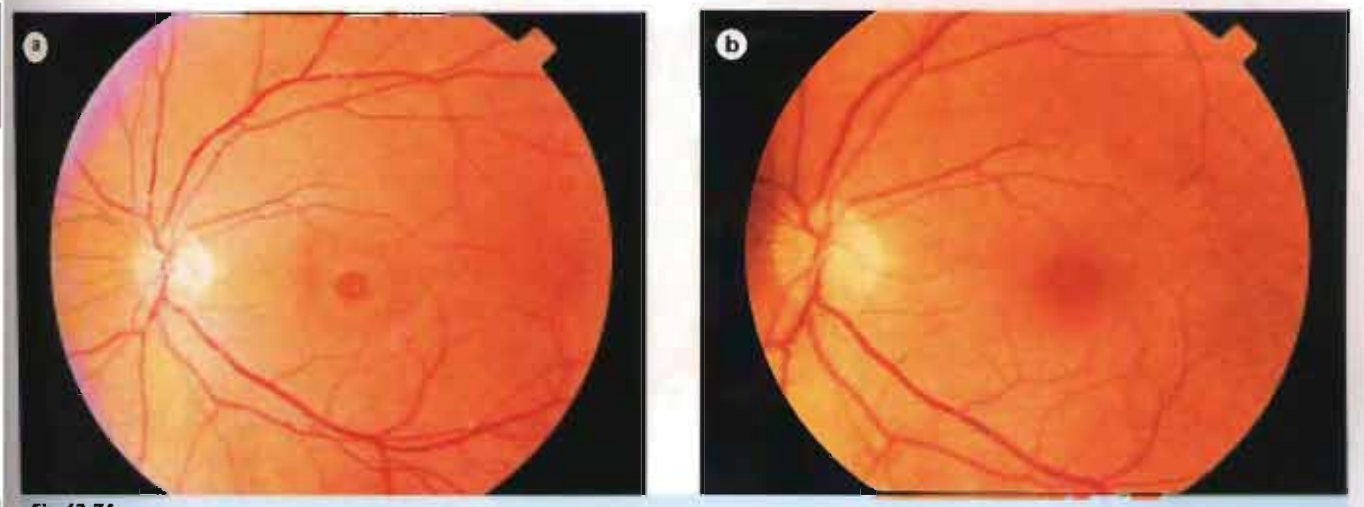


Fig. 13.76
(a) Full-thickness macular hole; (b) following successful closure (Courtesy of S. Milewski)

*b. **Blunt ocular trauma*** may cause a macular hole as a result of either vitreous traction or commotio retinae in which there is disruption of photoreceptors and subsequent hole formation.

2. **Macular pseudo-holes**
   *a. **Within premacular fibrosis*** (Fig. 13.77).
   *b. **Lamellar hole*** resulting from long-standing severe cystoid macular oedema.
   *c. **White dot fovea*** is an uncommon asymptomatic condition. White dots may be arranged diffusely or in the form of a ring along the margin of the foveola. The latter pattern simulates the appearance of a true macular hole with a cuff of fluid.

Central serous retinopathy

Central serous retinopathy (CSR, central serous chorioretinopathy) is a typically sporadic, self-limited disease of young or middle-aged adult males with type A personality. It is characterized by a usually unilateral, localized detachment of the sensory retina at the macula with or without associated PED. It is uncertain whether the primary pathology involves hyperpermeability of the RPE or the choroidal vasculature. Factors reported to induce or aggravate CSR include emotional stress, hypertension, systemic lupus erythematosus and the administration of systemic steroids.

Clinical features

1. **Presentation** is with unilateral blurred vision associated with a positive relative scotoma and micropsia and/or metamorphopsia. Occasionally the condition is extrafoveal and asymptomatic.
2. **Visual acuity** is usually reduced to 6/9–6/12 and often correctable to 6/6 with a weak 'plus' lens. The elevation of the sensory retina gives rise to an acquired hypermetropia with disparity between the subjective and objective refraction of the eye.

Fig. 13.77
Macular pseudo-hole within premacular fibrosis

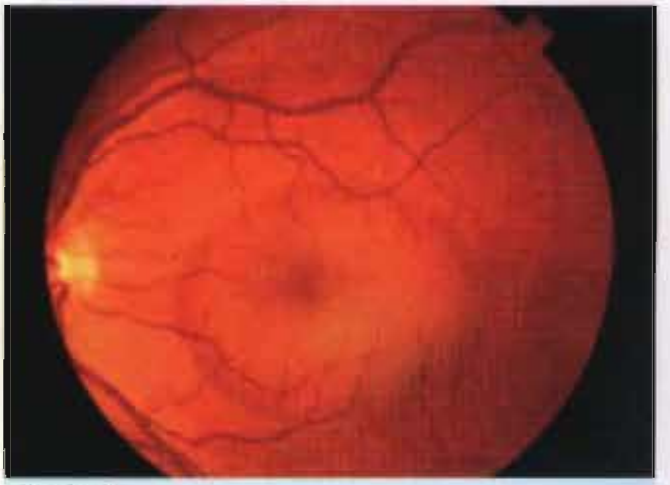


Fig. 13.78
Central serous retinopathy

3. **Fundus**
   - A round or oval detachment of the sensory retina is present at the posterior pole (Fig. 13.78).
   - The subretinal fluid may be clear or turbid and small precipitates may be present on the posterior surface of the sensory detachment.
   - Occasionally, an abnormal focus in the RPE, through which fluid has leaked from the choriocapillaris into the subretinal space, can be detected.
   - In some cases a small PED may be evident within the serous detachment.
4. **FA** shows one of the following pictures:
   *a. **Smoke-stack*** appearance which evolves as follows:
   - The early phase shows a small hyperfluorescent spot due to leakage of dye through the RPE (Fig. 13.79b). More than one leak may be present.
   - During the late venous phase, fluorescein passes into the subretinal space and ascends vertically (like a smoke-stack) (Fig. 13.79c) from the point of leakage until the upper border of the detachment.
   - The dye then spreads laterally, taking on a 'mushroom' or 'umbrella' configuration (Fig. 13.79d), until the entire area of detachment is filled.

   *b. **Ink-blot*** appearance is less common and evolves as follows:
   - The early phase shows a small hyperfluorescent spot (Fig. 13.80b).
   - The spot gradually enlarges centrifugally (Fig. 13.80c and d) until the entire detachment is filled with dye.

Course

1. **Short** course. Most commonly, spontaneous absorption of subretinal fluid occurs within 1–6 months with return to normal, or near normal, visual acuity.
2. **Prolonged** course. In some patients CSR lasts longer than 6 months but spontaneously resolves within 12 months. Even if visual acuity returns to normal, some degree of subjective visual impairment such as micropsia may persist, but seldom causes any significant disability.
3. **Chronic** course. In a minority of cases, the condition lasts longer than 12 months and is characterized by progressive RPE changes associated with a permanent impairment of visual acuity and the occasional development of CNV. FA shows granular hyperfluorescence with one or more leaks. This may be a consequence of either multiple recurrent attacks or prolonged detachment, although a minority of patients do not have a past history of typical CSR, and in some the changes are bilateral.

Treatment

Argon laser photocoagulation to the RPE leak or detachment achieves speedier resolution and lowers the recurrence rate but does not influence the final visual outcome. It is advisable to wait for 4 months before considering treatment of the first attack and 1 month for recurrences. Treatment is contraindicated if the leak is near or within the FAZ.

1. **Technique.** Two or three low- to moderate-intensity burns are applied to the leakage site (200 μm, 0.2 seconds) to produce mild greying of the RPE.

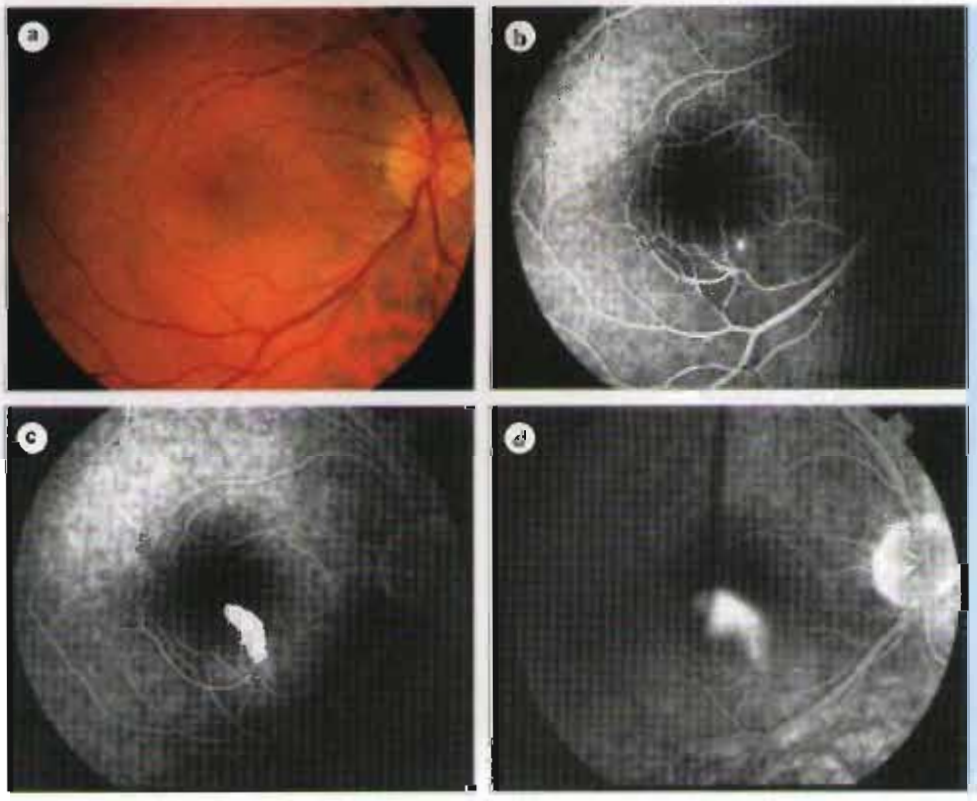


Fig. 13.79
(a) Central serous retinopathy; (b–d) FA showing a smoke-stack appearance (see *text*) (Courtesy of S. Milewski)

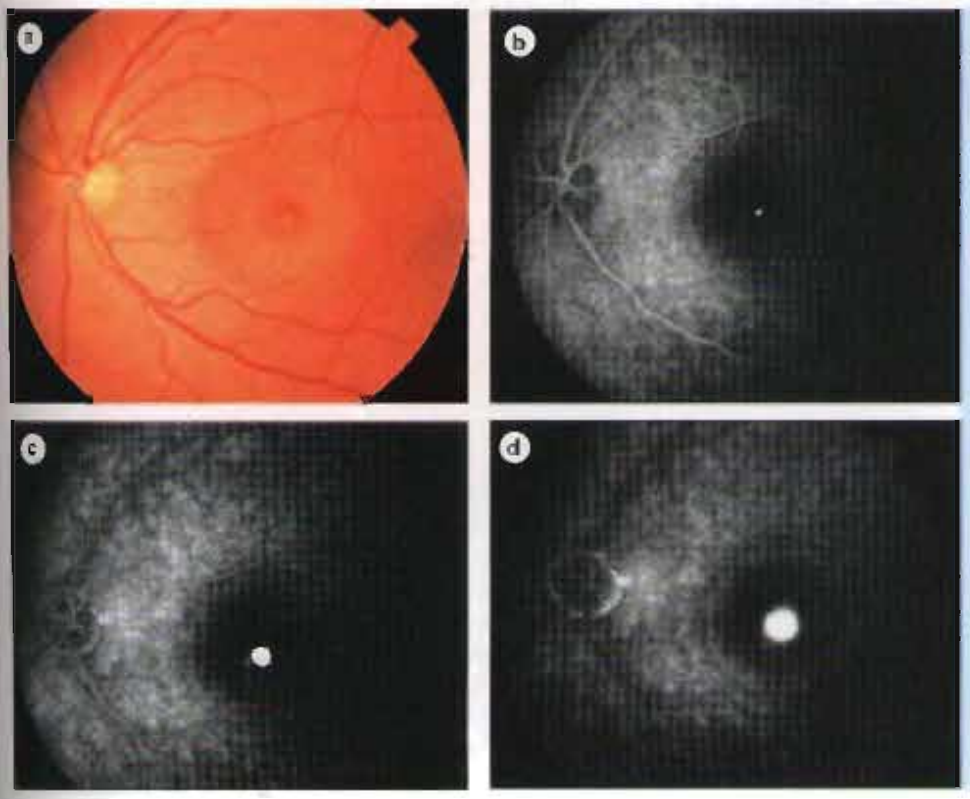


Fig. 13.80
(a) Central serous retinopathy; (b–d) FA showing an ink-blot appearance (Courtesy of S. Milewski)

2. **Careful follow-up** is required as 2–5% of treated eyes subsequently develop CNV.

Differential diagnosis of sensory macular detachment

1. **Congenital optic disc anomalies**, most frequently optic disc pit (*see* Fig. 13.111) and occasionally tilted disc, may be associated with serous macular detachment. Unless the optic disc is examined carefully the diagnosis may be missed.
2. **Choroidal tumours** with a predilection for the posterior pole such as circumscribed choroidal haemangioma and metastatic carcinoma.
3. **Unilateral acute idiopathic maculopathy** is a rare self-limiting condition that typically causes sudden unilateral visual loss in a young person.
4. **Choroidal neovascularization**, particularly if idiopathic.
5. **Harada disease** during the stage of multifocal detachments of the sensory retina may mimic multifocal CSR.

Cystoid macular oedema

Cystoid macular oedema (CMO) is the result of accumulation of fluid in the outer plexiform and inner nuclear layers of the retina centred about the foveola and the formation of fluid-filled cyst-like changes. In the short term, CMO is usually innocuous; long-standing cases, however, usually lead to coalescence of the fluid-filled microcysts into large cystoid spaces and subsequent lamellar hole formation at the fovea with irreversible damage to central vision (Fig. 13.81). CMO is a common and non-specific condition that may occur with any type of macular oedema.

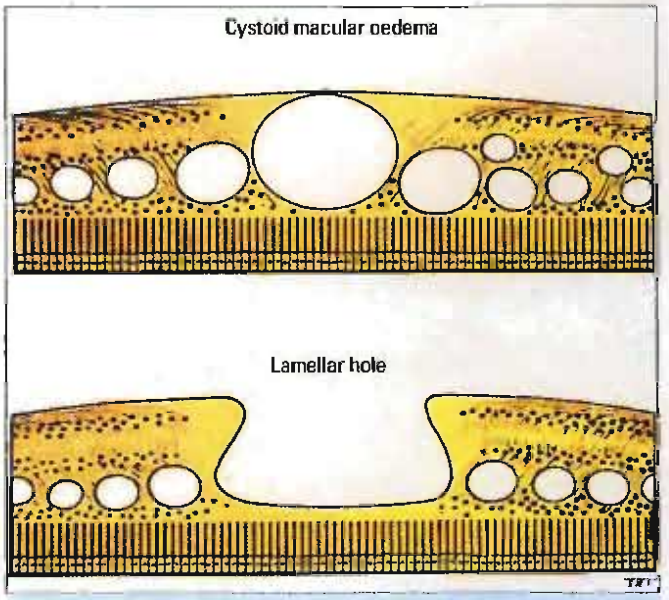


Fig. 13.81
Cystoid macular oedema resulting in lamellar hole formation

Clinical features

1. **Presentation** varies with the cause. Visual acuity may already be impaired by pre-existing disease such as branch vein occlusion. In other cases without pre-existing disease such as after cataract surgery, the patient complains of impairment of central vision associated with a positive central scotoma.
2. **Signs**
   - Slit-lamp biomicroscopy shows loss of the foveal depression, thickening of the retina and multiple cystoid areas in the sensory retina (Fig. 13.82).
   - In early cases cystoid changes may be difficult to discern and the main finding is a yellow spot at the foveola.
3. **FA**
   - The arteriovenous phase shows mild parafoveal hyperfluorescence due to early leakage (Fig. 13.83b).
   - The late venous phase shows increasing hyperfluorescence and coalescence of the focal leaks (Fig. 13.83c).
   - The late phase shows a 'flower-petal' pattern of hyperfluorescence (Fig. 13.83d) caused by accumulation of dye within microcystic spaces in the outer plexiform layer of the retina, with its radial arrangement of fibres about the centre of the foveola (Henle layer).

Fig. 13.82
Appearance of cystoid macular oedema on slit-lamp biomicroscopy

Causes and treatment

1. **Retinal vascular disease** (*see* Chapter 14).
   a. ***Causes*** include diabetic retinopathy, retinal vein occlusion, idiopathic retinal telangiectasia, retinal artery macroaneurysm and radiation retinopathy.
   b. ***Treatment*** by laser photocoagulation may be appropriate in selected cases.
2. **Intraocular inflammatory disease** (*see* Chapter 10).
   a. ***Causes*** include intermediate uveitis, birdshot retinochoroidopathy, multifocal choroiditis with panuveitis, toxoplasmosis, cytomegaloviral retinitis, Behçet disease and scleritis.
   b. ***Treatment*** is aimed at controlling the inflammatory process with steroids or immunosuppressive agents. Systemic carbonic anhydrase inhibitors may be beneficial in CMO associated with intermediate uveitis.

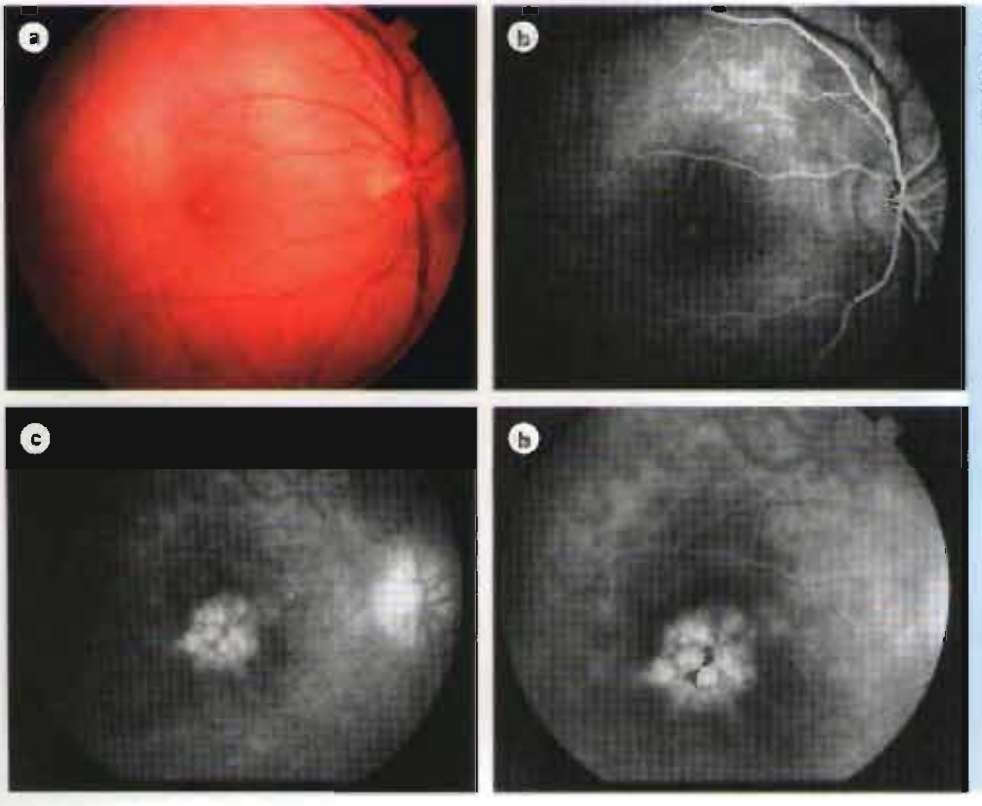


Fig. 13.83
(a) Cystoid macular oedema; (b–d) FA showing leakage (see text)
(Courtesy of S. Milewski)

3. **Post-cataract surgery**. CMO is rare following uncomplicated surgery and usually resolves spontaneously.
   a. *Risk factors* for visually significant CMO include anterior chamber IOL implantation, secondary lens implantation, operative complications such as posterior capsular rupture, vitreous loss and vitreous incarceration into the incision site, diabetes and a history of CMO in the other eye. Peak incidence is at 6–10 weeks after surgery, although the interval may be much longer.
   b. *Treatment* involves correction of the underlying cause, if possible. For example, vitreous incarceration in the anterior segment may be amenable to anterior vitrectomy or YAG laser disruption of vitreous adhesions. As a last resort it may be necessary to remove an anterior chamber IOL. If a correctable cause is not present, treatment is difficult although many cases resolve spontaneously within 6 months. Treatment of persistent CMO involves the following measures:
      - Systemic carbonic anhydrase inhibitors.
      - Steroids, given topically or by posterior periocular injection, combined with topical non-steroidal anti-inflammatory drugs (NSAIDs) such as ketorolac 0.5% (Acular) administered q.i.d. may be beneficial even in long-standing and clinically significant CMO. Unfortunately, in many cases CMO recurs when treatment is discontinued, so that long-term medication may be required.
      - Pars plana vitrectomy may be useful for CMO refractory to medical therapy even in eyes without apparent vitreous disturbance.
4. **After other surgical procedures**
   a. *Causes* include YAG laser capsulotomy, peripheral retinal cryotherapy and laser photocoagulation. The risk of CMO is reduced if capsulotomy is delayed for 6 months or more after cataract surgery. Rarely, CMO may develop following scleral buckling, penetrating keratoplasty and glaucoma filtration surgery.
   b. *Treatment* is unsatisfactory although the CMO is often mild and self-limited.
5. **Drug-induced**
   a. *Causes* include topical adrenaline 2% especially in the aphakic eye, topical latanoprost and systemic nicotinic acid.
   b. *Treatment* involves cessation of medication.
6. **Retinal dystrophies** (*see* Chapter 15).
   a. *Causes* include retinitis pigmentosa, gyrate atrophy and dominantly inherited CMO.
   b. *Treatment* with systemic carbonic anhydrase inhibitors may be beneficial in CMO associated with retinitis pigmentosa.
7. **Vitreomacular traction syndrome** is characterized by partial peripheral vitreous separation with persistent posterior attachment to the macula. This results in anteroposterior and tangential traction vectors. Chronic CMO due to anteroposterior traction is common and may respond to vitrectomy.
8. **Macular epiretinal membranes** may occasionally cause CMO by disrupting the perifoveal capillaries. Surgical excision of the membrane may be beneficial in selected cases.

Myopic maculopathy

High myopia is associated with progressive, excessive elongation of the globe often followed by degenerative changes involving the sclera, choroid, Bruch membrane, RPE and sensory retina. Fundus changes usually occur when the myopia measures 6 D or more and the axial length 25 mm or more.

General changes

- The optic disc is often tilted and may be surrounded by chorioretinal atrophy (Fig. 13.84)
- A pale tessellated appearance due to attenuation of the RPE.
- Severe chorioretinal atrophy involving the posterior pole characterized by visibility of the larger choroidal vessels and eventually the sclera.
- Peripheral chorioretinal atrophy (pavingstone degeneration) (*see* Fig. 12.73).

Macular changes

1. **Geographic atrophy** of the RPE and choriocapillaris (Fig. 13.85).
2. **'Lacquer cracks'** develop in about 5% of highly myopic eyes. They represent large breaks in Bruch membrane and are characterized by fine, irregular, yellow lines, often branching and criss-crossing (Fig. 13.86).

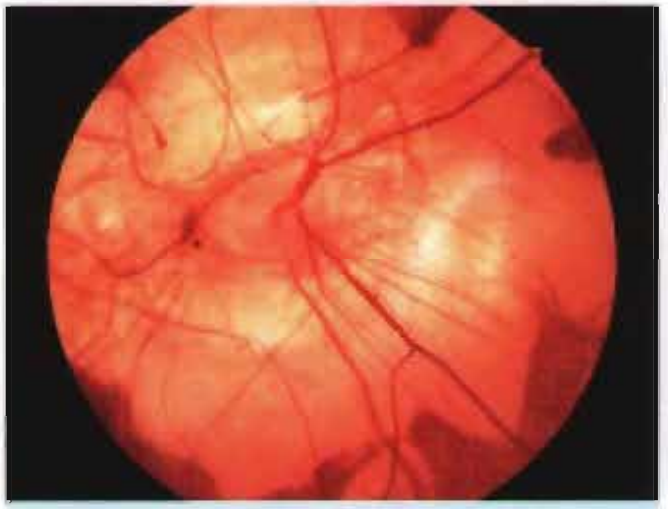


Fig. 13.84
Tilted optic disc with myopic chorioretinal atrophy

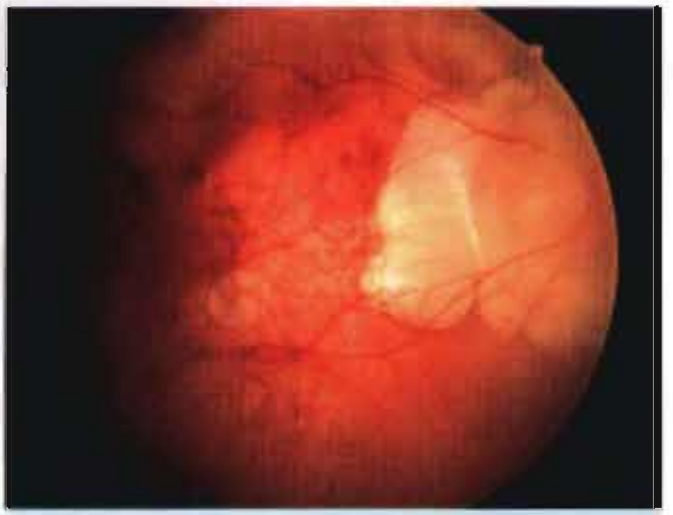


Fig. 13.85
Geographic atrophy of the RPE and choriocapillaris at the macula and severe parapapillary chorioretinal atrophy in high myopia

Fig. 13.87
Subretinal haemorrhage from CNV in high myopia

Fig. 13.86
Lacquer cracks in high myopia

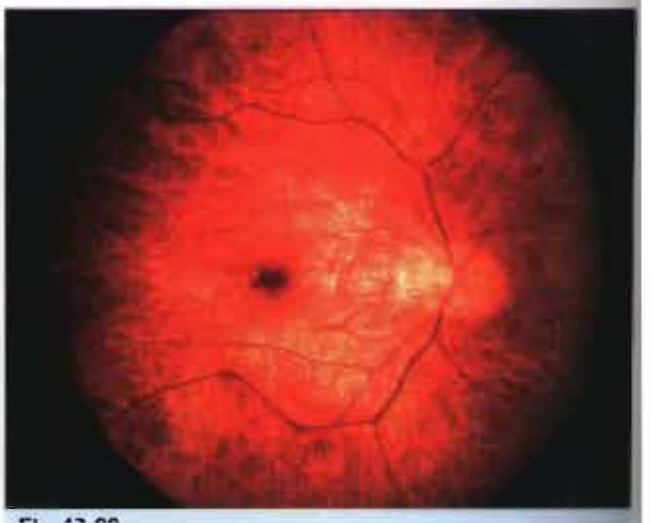


Fig. 13.88
Small, fovea 'coin' haemorrhage not associated with CNV in high myopia

3. **Exudative** maculopathy secondary to CNV associated with 'lacquer cracks' (Fig. 13.87). The prognosis for central vision is, however, better than in exudative AMD because CNV in highly myopic eyes tends to be relatively self-limited and not associated with subretinal fibrovascular scarring.
4. **Subretinal 'coin' haemorrhages** may develop from lacquer cracks in the absence of CNV and are usually transient (Fig. 13.88).
5. **Foerster–Fuchs spot** is a raised, circular, pigmented lesion that may develop after a macular haemorrhage has absorbed (Fig. 13.89).
6. **Macular hole**, which unlike an age-related macular hole, may result in retinal detachment.

Fig. 13.89
Foerster–Fuchs spot in high myopia

Associations of high myopia

1. **Ocular**
   - Retinal detachment due to a combination of vitreous degeneration, lattice degeneration and retinal breaks (macular holes, atrophic peripheral holes and tears) (*see* Chapter 12).
   - Cataract (posterior subcapsular or early-onset nuclear sclerosis).
   - Increased prevalence of primary open-angle glaucoma, pigmentary glaucoma and steroid responsiveness.
   - Retinopathy of prematurity may be associated with the subsequent development of myopia.
2. **Systemic** associations include Stickler, Marfan, Ehlers-Danlos and Pierre–Robin syndromes.

Macular epiretinal membrane

Macular epiretinal membranes (epiretinal gliosis) that develop at the vitreoretinal interface consist of proliferations of retinal glial cells which have gained access to the retinal surface through breaks in the internal limiting membrane. Such breaks may be created when the posterior vitreous detaches from the macula. The clinical appearance of an epiretinal membrane depends on its density and any associated distortion of the retinal vasculature. It is convenient to divide the condition into: (a) *cellophane maculopathy* and (b) *macular pucker*.

Causes

1. **Idiopathic** membranes affect otherwise healthy elderly individuals and are bilateral in about 10% of cases.
2. **Secondary**
   a. ***Retinal procedures*** such as detachment surgery, photocoagulation and cryotherapy may either induce or worsen pre-existing macular epiretinal gliosis. Untreated, such membranes usually cause variable but permanent reduction of vision. Very occasionally, however, a membrane may separate spontaneously from the retina.
   b. ***Other causes*** include retinal vascular disease, intraocular inflammation and ocular trauma.

Cellophane maculopathy

This is caused by a thin translucent layer of epiretinal cells. It is common and usually idiopathic.

1. **Presentation** may be with mild metamorphopsia although frequently the condition is asymptomatic and discovered by chance.
2. **Visual acuity** may be normal or slightly reduced (6/9).
3. **Fundus**
   - Irregular light reflex or sheen at the macula (Fig. 13.90a).
   - The membrane itself is translucent and best detected with 'red-free' light. However, as it thickens and contracts it becomes more obvious and causes fine striae on the retinal surface and distortion of blood vessels which is highlighted on FA (Fig. 13.90b).
4. **Treatment** is not necessary.

Macular pucker

This is caused by thickening and contraction of the membrane. It is less common than cellophane maculopathy and may be idiopathic or secondary.

1. **Presentation** is with metamorphopsia and blurring of central vision.
2. **Visual acuity** is 6/12 or worse, depending on severity.
3. **Fundus**
   - Retinal wrinkling and white striae may obscure the underlying markedly tortuous retinal vasculature (Fig. 13.91a and b).
   - Associated findings include macular pseudo-holes within the membrane (*see* Fig. 13.77) and occasionally secondary chronic CMO.
4. **Pattern-reversal** visually evoked potential latencies are prolonged and amplitude is reduced.
5. **Treatment** by peeling of the membrane from the retinal surface often improves or eliminates distortion, and may improve visual acuity.

Fig. 13.90
Cellophane maculopathy (see text)
(Courtesy of Wilmer Institute)

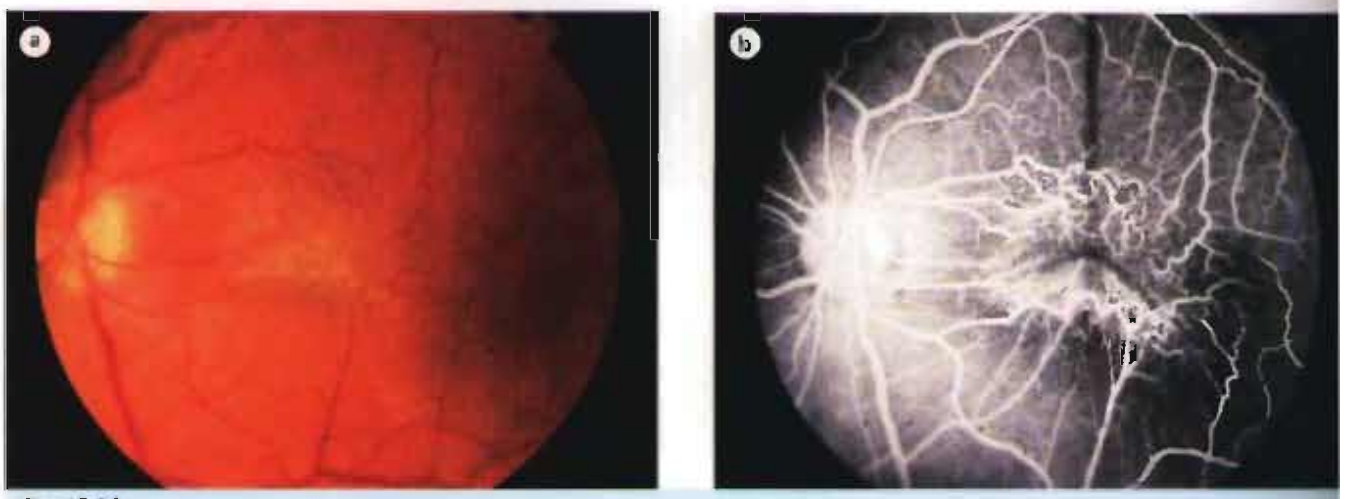


Fig. 13.91
Macular pucker *(see text)*

Angioid streaks

Angioid streaks represent crack-like dehiscences in the elastic layer of Bruch membrane due to an abnormal fragility of the lamina basalis caused by a degenerative process combined with calcium deposition. This results in secondary changes in the RPE and choriocapillaris.

Clinical features

1. Fundus

- Linear, reddish-brown lesions with irregular serrated edges lie beneath the normal retinal blood vessels. They may initially be very subtle and easily overlooked (Fig. 13.92).
- Later they become more obvious due to secondary RPE atrophy or hyperplasia (Fig. 13.93).
- The streaks intercommunicate in a ring-like fashion around the optic disc and then radiate outwards from the parapapillary area.
- 'Peau d'orange' (orange skin) is pigmentary mottling at the posterior pole, most apparent temporal to the macula, and may antedate the appearance of angioid streaks.
- Salmon spots consisting of peripheral, focal chorioretinal scars may be present (Fig. 13.94).
- Optic nerve anomalies, occasionally present, include optic disc drusen (Fig. 13.95) and vascular loops.

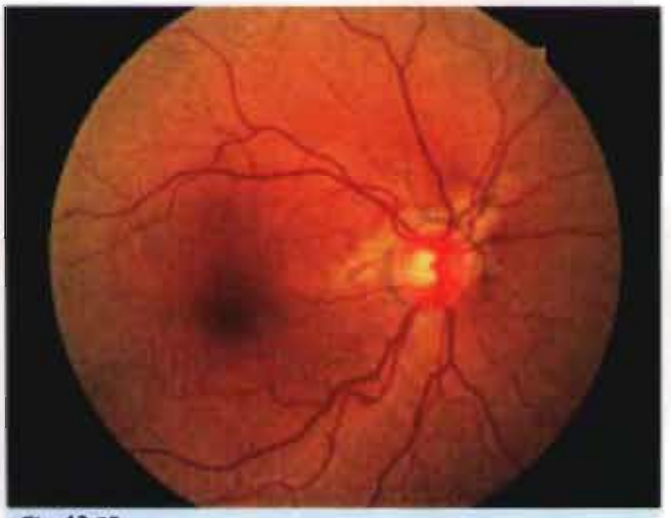


Fig. 13.92
Mild angioid streaks with extensive 'peau d'orange'

Fig. 13.93
Advanced angioid streaks

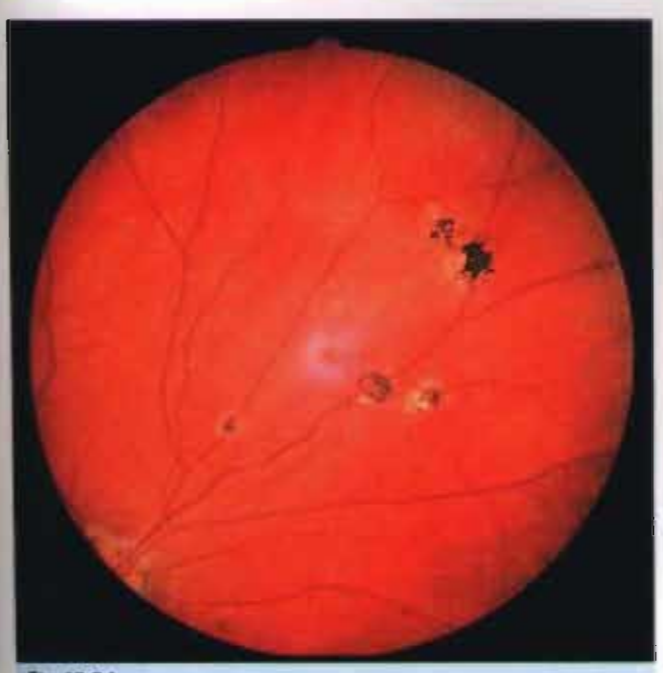


Fig. 13.94
Peripheral, focal, chorioretinal scars ('salmon spots') in an eye with angioid streaks

Fig. 13.95
Optic disc drusen in an eye with angioid streaks

2. **FA** shows hyperfluorescence due to RPE window defects over the streaks (Fig. 13.96d) and is also useful in detecting CNV (Fig. 13.96c).

Prognosis

This is guarded because visual impairment occurs in over 70% of patients due to:

1. **Exudative maculopathy** due to CNV (*see* Fig. 13.96a and c). Early treatment of CNV by laser photocoagulation may be appropriate in selected cases but carries a high risk of recurrence.
2. **Choroidal haemorrhage** may occur on trivial ocular trauma and result in a subfoveal haemorrhage (Fig. 13.97) and subsequent scarring (Fig. 13.98). Since these eyes are fragile patients should be advised not to participate in contact sports.
3. **Foveal involvement** by a streak.

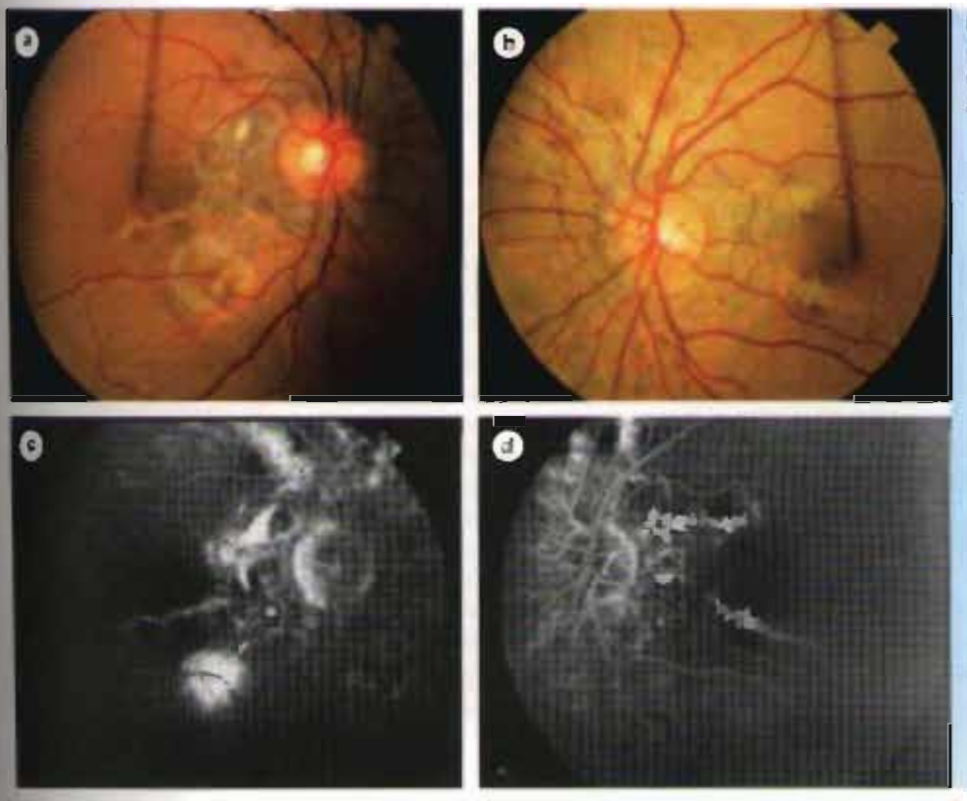


Fig. 13.96
(**a** and **c**) Angioid streaks and CNV; (**b** and **d**) angioid streaks alone (*see text*) (Courtesy of S. Milewski)

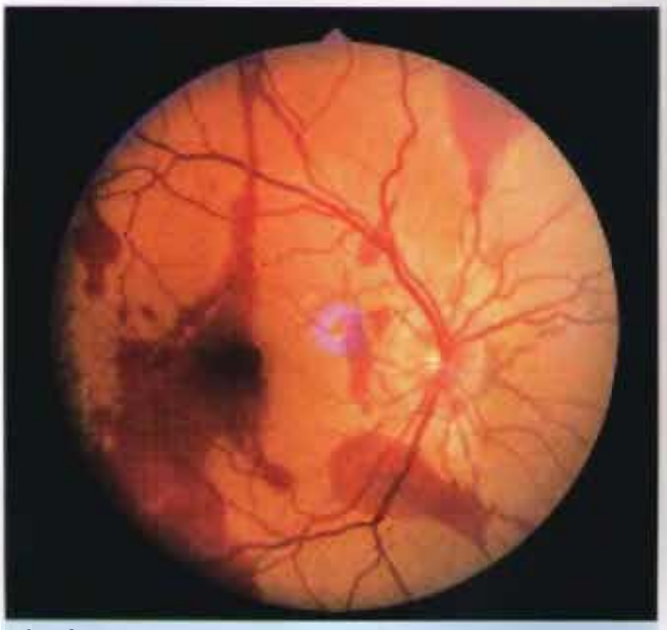


Fig. 13.97
Traumatic choroidal rupture and haemorrhage associated with angioid streaks

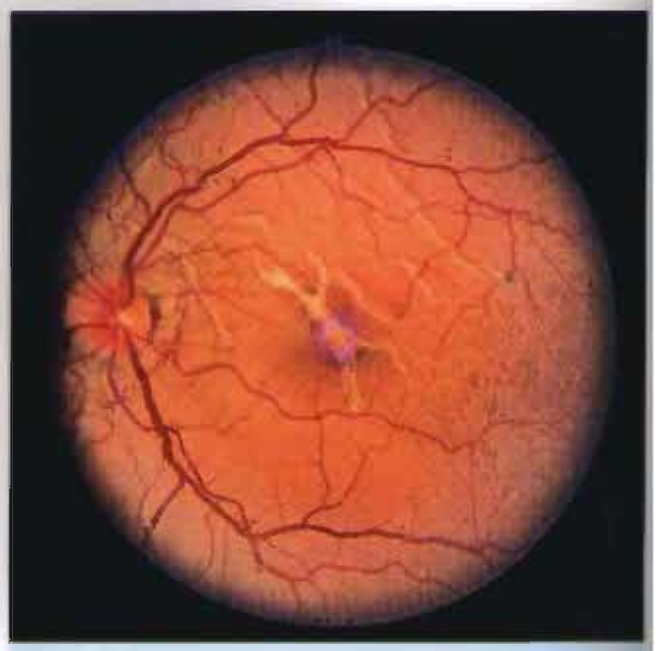


Fig. 13.98
Subretinal scarring following absorption of haemorrhage associated with angioid streaks

Systemic associations

Approximately 50% of patients have one of the following diseases:

1. **Pseudoxanthoma elasticum** (PXE) is by far the most common. Approximately 85% of patients develop ocular involvement, usually after the second decade of life. The combination of the two is referred to as *'Groenblad–Strandberg syndrome'* (*see* Chapter 20).
2. **Ehlers–Danlos syndrome type 6** (ocular sclerotic) is an uncommon association (*see* Chapter 20).
3. **Other** rare associations include Paget disease and certain haemoglobinopathies.

Choroidal folds

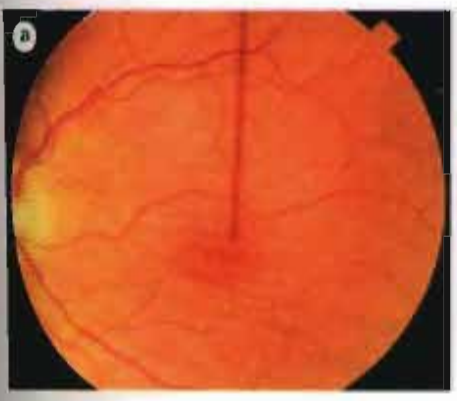
Choroidal folds are parallel grooves or striae involving the inner choroid, Bruch membrane, the RPE and sometimes the sensory retina. Possible mechanisms include choroidal congestion, scleral folding and contraction of Bruch membrane.

Causes

1. **Idiopathic** folds may occur in both eyes of healthy hypermetropic patients with normal or near-normal visual acuity.
2. **Orbital diseases** such as retrobulbar tumours and thyroid eye disease.
3. **Choroidal tumours** such as melanomas may mechanically displace the surrounding choroid and cause folding.
4. **Ocular hypotony** following filtration surgery, if severe and prolonged.
5. **Miscellaneous** causes include chronic papilloedema, posterior scleritis and scleral buckling for repair of retinal detachment.

Clinical features

1. **Presentation** may be with metamorphopsia although the patient may be asymptomatic. Initially visual dysfunction is caused by distortion of overlying retinal receptors. In long-standing cases, permanent changes may develop in the RPE and sensory retina.
2. **Visual acuity** may be normal or impaired, depending on aetiology and duration.
3. **Fundus**
   - Parallel grooves, usually horizontally orientated (Fig. 13.99a); occasionally vertical, oblique or irregular.
   - The crests (elevated portions) appear paler due to thinning of the RPE and the troughs darker due to RPE compression.
4. **FA** shows alternating hyperfluorescent and hypofluorescent streaks at the level of the RPE (Fig. 13.99b). Hyperfluorescence corresponds to the crests due to increased background choroidal fluorescence showing through the thinned RPE. Hypofluorescence corresponds to the troughs due to blockage of choroidal fluorescence by the compressed RPE (Fig. 13.100).



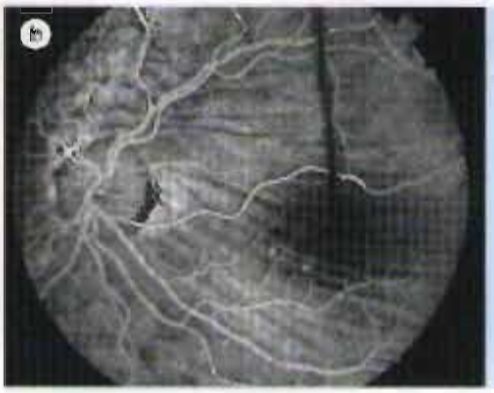


Fig. 13.99
Choroidal folds (see text) (Courtesy of S. Milewski)

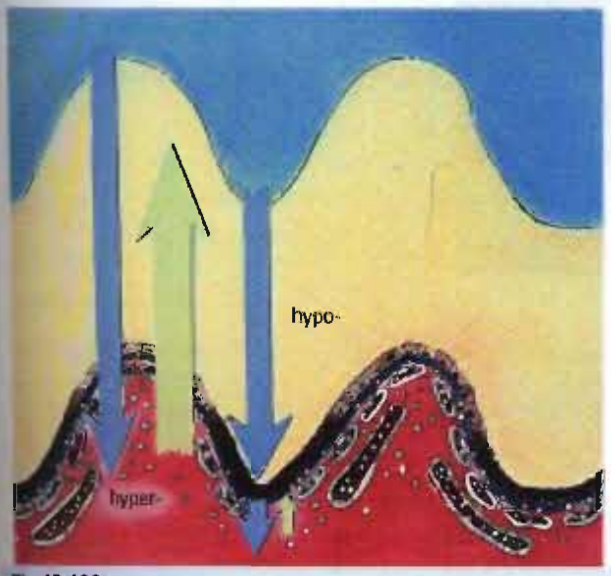


Fig. 13.100
Mechanisms of hypo- and hyperfluorescence in choroidal folds

Drug-induced maculopathies

Antimalarials

Chloroquine (Nivaquine, Avlocor) and hydroxychloroquine (Plaquenil) are quinolone derivatives used in the prophylaxis and treatment of malaria as well as in the treatment of rheumatoid arthritis, systemic lupus erythematosus and cutaneous lupus. Chloroquine has also been advocated for the treatment of calcium abnormalities of sarcoidosis. Antimalarials are excreted from the body very slowly and are melanotropic drugs that become concentrated in melanin-containing structures of the eye such as the RPE and choroid. The two main ocular side effects of antimalarials are retinotoxicity and corneal deposits. Although uncommon, the retinal changes are potentially serious and the corneal changes (vortex keratopathy), which are extremely common, are innocuous (*see* Fig. 5.135).

1. **Chloroquine** retinotoxicity is related to total cumulative dose. The normal daily dose is 250 mg. A cumulative dose of less than 100 g or duration of treatment under 1 year is rarely associated with retinal damage. The risk of toxicity increases significantly when the cumulative dose exceeds 300 g (i.e. 250 mg daily for 3 years). However, there have been reports of patients receiving cumulative doses exceeding 1000 g without developing retinotoxicity. If possible, chloroquine should be used only if other agents are ineffective.
2. **Hydroxychloroquine** is safer than chloroquine and provided the daily dose does not exceed 400 mg the risk of retinotoxicity is negligible. Physicians should therefore be encouraged to use hydroxychloroquine instead of chloroquine whenever possible.

Chloroquine maculopathy

1. **Premaculopathy** is characterized by normal visual acuity but loss of the foveal reflex. This is followed by the development of fine granular changes at the macula which may be associated with mild abnormalities of colour vision and small scotomas to a red target on the Amsler grid. Premaculopathy is reversible if the drug is discontinued.
2. **Early maculopathy** is characterized by a modest reduction of visual acuity (6/9–6/12). Fundus examination shows a subtle macular lesion characterized by central foveolar pigmentation surrounded by a depigmented zone of RPE atrophy which is in turn encircled by a hyperpigmented ring (Fig. 13.101a). The lesion may be more obvious on FA than ophthalmoscopy because the RPE atrophy gives rise to a 'window' defect (Fig. 13.101b–d). This stage is irreversible even if the drug is stopped.
3. **Established maculopathy** is characterized by moderate reduction of visual acuity (6/18–6/24) and an obvious 'bull's eye' macular lesion.

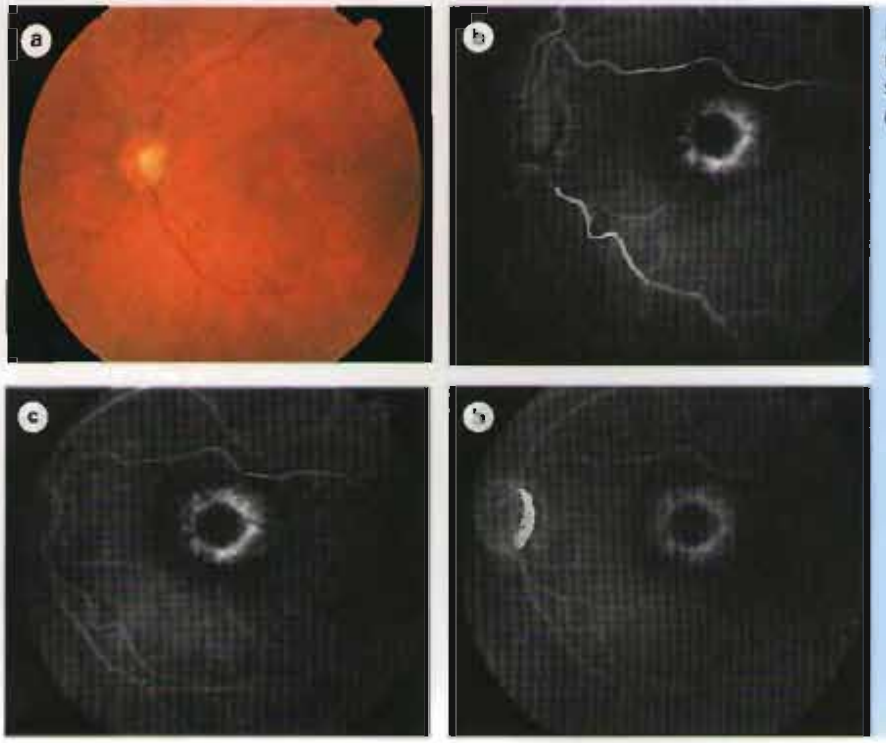


Fig. 13.101
(a) Chloroquine maculopathy; (b–d) FA showing bull's eye maculopathy (see text)
(Courtesy of S. Milewski)

4. **Severe maculopathy** is characterized by marked reduction of visual acuity (6/36–6/60) with widespread RPE atrophy surrounding the fovea (Fig. 13.102).
5. **End-stage maculopathy** is characterized by severe reduction of visual acuity and marked atrophy of the RPE with unmasking of the larger choroidal blood vessels. The retinal arterioles may also become attenuated and pigment clumps develop in the peripheral retina (Fig. 13.103).

Screening

Screening of patients on hydroxychloroquine is unnecessary. In clinical practice chloroquine may also be administered safely to patients without the need for repetitive routine examinations by ophthalmologists or the use of complicated tests. Recording of visual acuity and ophthalmoscopy by the prescribing doctor is all that is required. The patient should be given an Amsler grid to use once a week. If an abnormality is

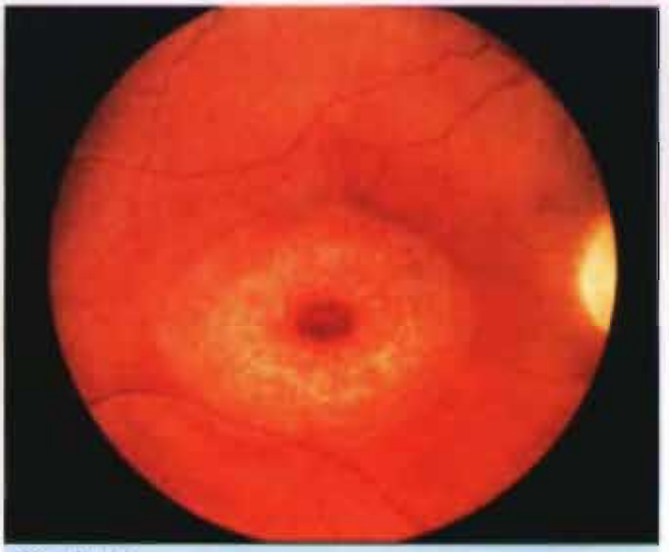


Fig. 13.102
Severe chloroquine maculopathy

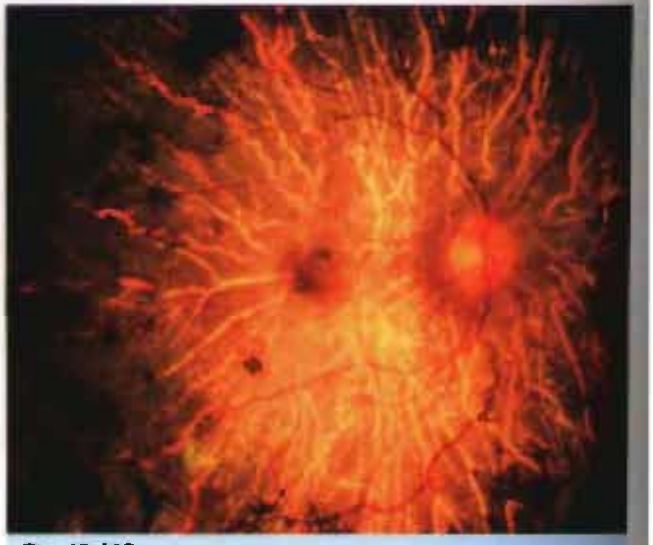


Fig. 13.103
End-stage chloroquine maculopathy

found, then ophthalmic referral should be sought. The ophthalmologist can then, if necessary, perform more sophisticated tests such as visual fields, macular threshold, colour vision testing, contrast sensitivity, FA and electro-oculography.

Phenothiazines

Thioridazine

Thioridazine (Melleril) is used to treat schizophrenia and related psychoses. The normal daily dose is 150–600 mg. Doses exceeding 800 mg/day for even a few weeks may be sufficient to impair visual acuity and dark adaptation. The clinical signs of progressive retinotoxicity are as follows:

- 'Salt-and-pepper' pigmentary disturbance involving the mid-periphery and posterior pole.
- Coarse plaque-like pigmentation and focal loss of the RPE and choriocapillaris (Fig. 13.104).
- Diffuse loss of the RPE and choriocapillaris (Fig. 13.105).

Chlorpromazine

Chlorpromazine (Largactil) is used as a sedative and to treat schizophrenia. The normal daily dose is 75–300 mg. Retinotoxicity may occur with larger doses over a prolonged period and is characterized by non-specific pigmentary granularity and clumping. Other innocuous ocular side effects include yellowish-brown granules on the anterior lens capsule (*see* Fig. 8.21) and corneal endothelial deposits.

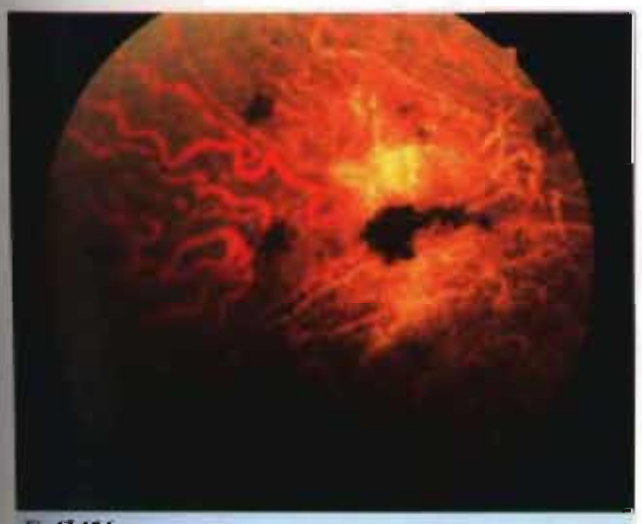


Fig. 13.104
Pigment plaques in thioridazine toxicity

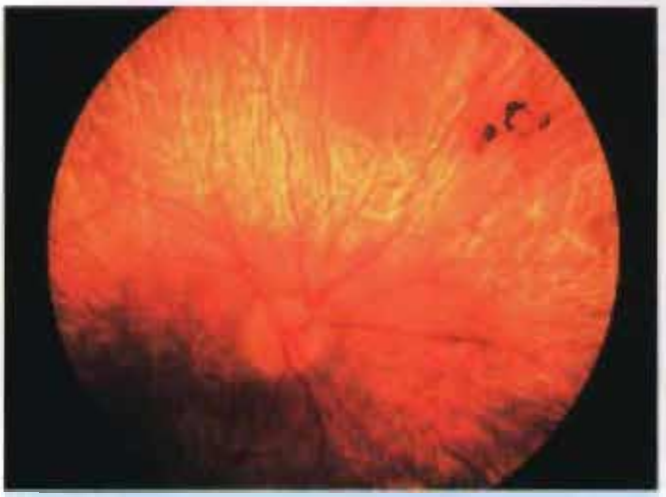


Fig. 13.105
Diffuse atrophy of the RPE and choriocapillaris in severe thioridazine toxicity

Toxic crystalline maculopathies

Tamoxifen

Tamoxifen (Nolvodex, Emblon, Noltan, Tamofen) is a specific anti-oestrogen used in the treatment of selected patients with breast carcinoma. It has few systemic side effects and ocular complications are rare on a normal daily dose of 20–40 mg. Retinotoxicity may occasionally develop in patients on higher doses and is characterized by relatively innocuous, bilateral, multiple, yellow, crystalline, ring-like deposits at the maculae (Fig. 13.106) which persist on cessation of treatment. Other rare ocular side effects are vortex keratopathy and optic neuritis, which are reversible on cessation of therapy. Because maculopathy is rare, routine screening is not warranted.

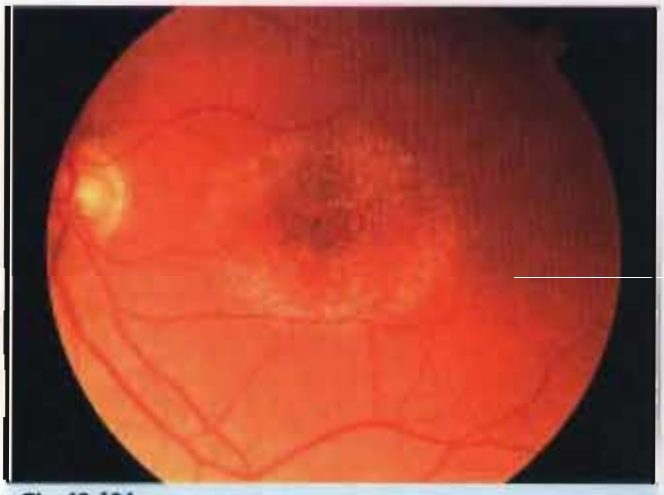


Fig. 13.106
Tamoxifen maculopathy (Courtesy of J. Salmon)

Canthaxanthin

This carotenoid is used to enhance sun tanning. Over prolonged periods it may cause the deposition of bilateral, tiny, glistening, yellow deposits, arranged symmetrically in a doughnut shape at the posterior poles (Fig. 13.107). The deposits are located in the superficial retina and are innocuous.

Methoxyflurane

Methoxyflurane (Penthrane) is an inhalant general anaesthetic. It is metabolized to oxalic acid, which combines with calcium to form the insoluble salt calcium oxalate, which is deposited in tissues including the RPE. Prolonged administration may lead to renal failure and secondary hyperoxalosis. It may also result in the formation of innocuous crystals within the retinal vasculature.

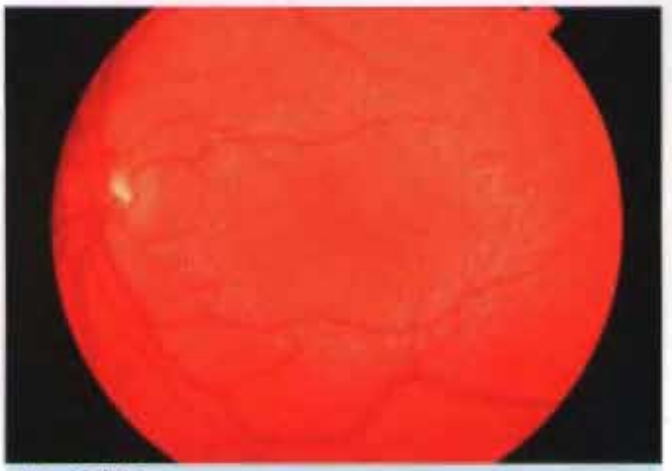


Fig. 13.107
Canthaxanthin maculopathy

2. **Presentation** is with sudden unilateral visual impairment.
3. **Signs**
   - Serosanguinous detachments of the RPE which may be multiple and variable in size and which may be associated with subretinal lipid (Fig. 13.108).
   - In some cases bullous retinal detachment and vitreous haemorrhage may occur.
4. **ICG** shows the presence of large choroidal vascular complexes with localized terminal polyp-like bulbs (Fig. 13.109) that fill slowly and then leak intensely.
5. **Treatment** by laser photocoagulation is occasionally required if serosanguinous leakage threatens the fovea.
6. **Prognosis** is generally good with spontaneous resolution of exudation and haemorrhage.

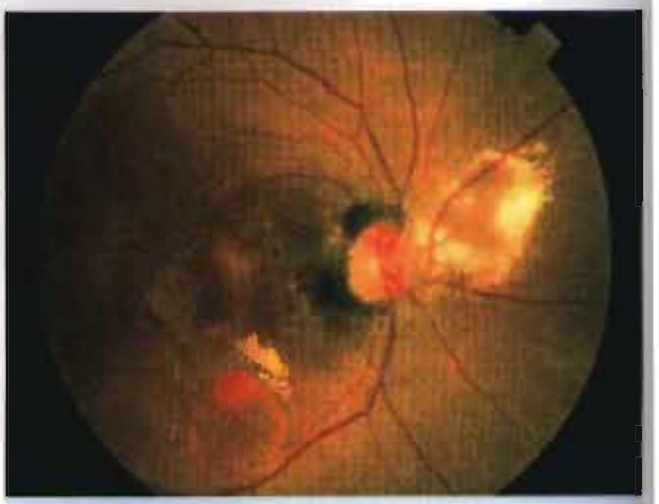


Fig. 13.108
Idiopathic polypoidal choroidal vasculopathy (Courtesy of R. Spaide)

Miscellaneous maculopathies

Idiopathic polypoidal choroidal vasculopathy

Idiopathic polypoidal choroidal vasculopathy (posterior uveal bleeding syndrome, multiple serosanguinous RPE detachment syndrome) is an uncommon condition with a predilection for non-white people.

1. **Pathogenesis**. There is an abnormality of the inner choroidal vessels consisting of a dilated network and multiple terminal aneurysmal protuberances in a polypoidal configuration, with a predilection for the macula and less frequently the parapapillary area. These polypoidal lesions appear to be responsible for episodic leakage and bleeding under the RPE and sensory retina.

Fig. 13.109
ICG of idiopathic polypoidal choroidal vasculopathy showing hyperfluorescent polyp-like bulbs (Courtesy of V. Tanner)

Maculopathy in optic disc pit

Optic disc pit is a rare, usually unilateral, congenital anomaly.

1. **Signs**
   - Visual acuity is normal in the absence of maculopathy.
   - The optic disc is larger than normal and contains a round or oval pit of variable size which is usually located temporally (Fig. 13.110), but may be central.
2. **Visual field defects** are common and may mimic those due to glaucoma.
3. **FA** of the pit shows early hypofluorescence and late hyperfluorescence (Fig. 13.111b).
4. **Maculopathy** (Fig. 13.111a and c) occurs in about 45% of eyes with non-central pits, most frequently at about puberty. Subretinal fluid is thought to be derived either from the vitreous or the subarachnoid space. A less likely source is leakage from abnormal blood vessels within the base of the pit (Fig. 13.111d). Initially there is a schisis-like separation of the inner retinal layers which communicates with the pit. This is followed by detachment of the outer retinal layers from the RPE.
5. **Treatment options**
   a. ***Observation*** at 3-monthly intervals for evidence of spontaneous resolution, which occurs in up to 25% of cases.
   b. ***Argon laser photocoagulation*** may be considered if visual acuity is deteriorating. The burns are applied along the temporal aspect of the disc. The success rate is about 30%.

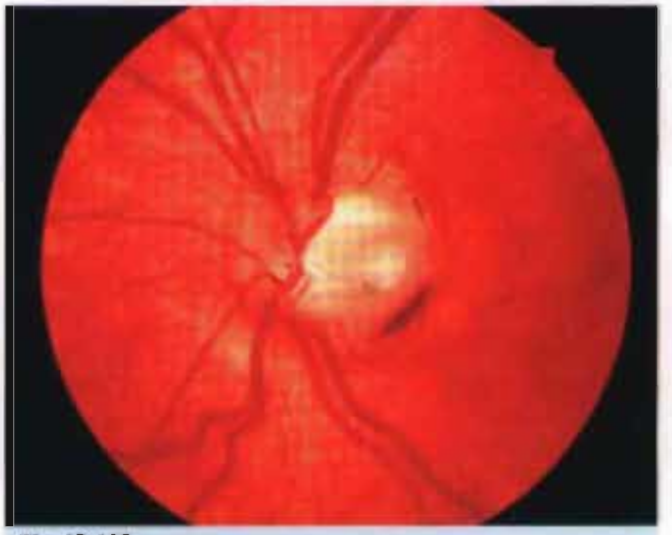


Fig. 13.110
Congenital optic disc pit

   c. ***Pars plana vitrectomy*** with air–fluid exchange, postoperative prone positioning and subsequent laser photocoagulation may be considered if laser alone is unsuccessful. The success rate is about 65%.
   d. ***Gas injection*** (C_3F_8) without vitrectomy may also be successful.

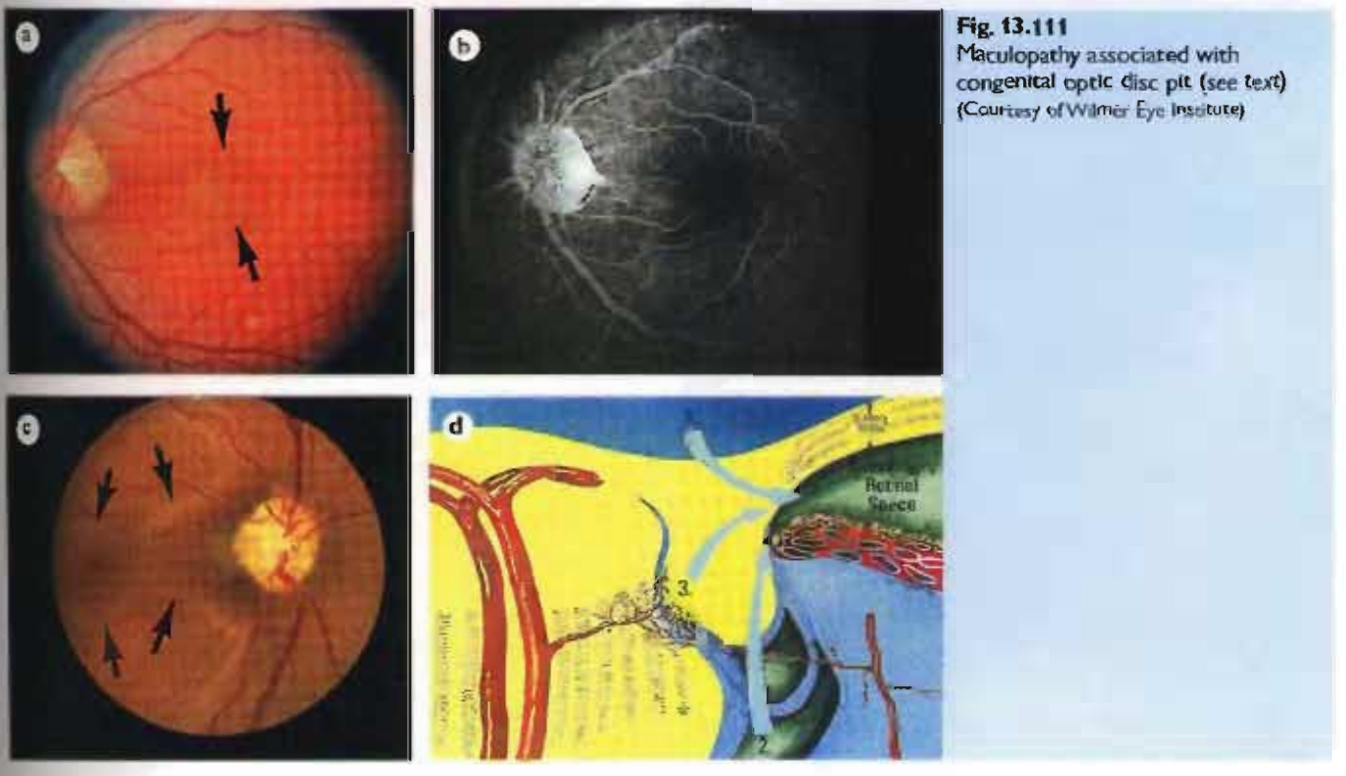


Fig. 13.111
Maculopathy associated with congenital optic disc pit (see text)
(Courtesy of Wilmer Eye Institute)

Solar maculopathy

Solar maculopathy is caused by photochemical effects of solar radiation as a result of directly or indirectly looking at the sun.

1. **Presentation** is 1–4 hours after solar exposure with unilateral or bilateral impairment of central vision, metamorphopsia or central scotomas.
2. **Signs**
   - Visual acuity is variably impaired according to the extent of damage.
   - Initially there are small, unilateral or bilateral, yellow foveolar spots with a grey margin (Fig. 13.112).
   - This is followed about 2 weeks later by circumscribed RPE mottling (Fig. 13.113) or a lamellar hole.
3. **Prognosis** is usually good with improvement of visual acuity to normal or near-normal levels within 6 months although mild symptoms may persist.

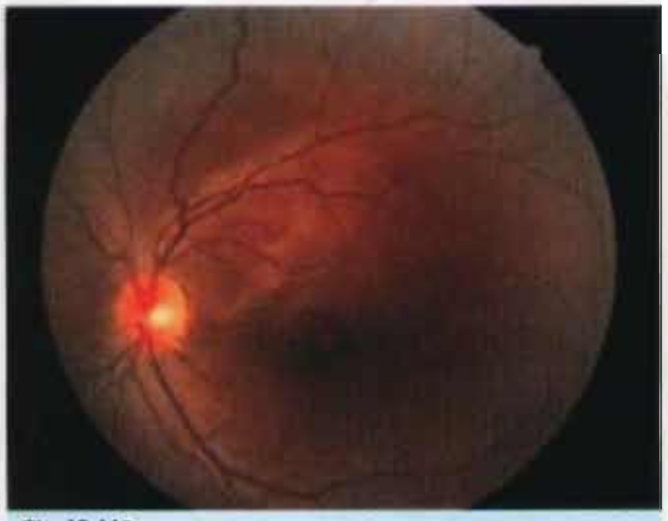


Fig. 13.112
Acute solar maculopathy showing a small yellow foveolar spot

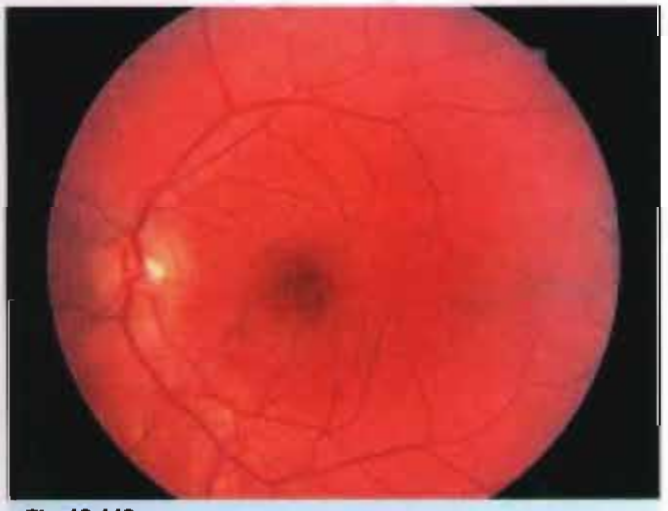


Fig. 13.113
Late solar maculopathy showing mild RPE mottling

Cancer-associated retinopathy

Cancer-associated retinopathy (CAR) is a rare autoimmune photoreceptor destruction in which patients develop visual disturbances in the absence of ocular metastases or involvement of visual pathways. CAR primarily occurs in patients with small cell lung carcinoma and occasionally other epithelial tumours. In 50% of cases it is the initial manifestation of the underlying tumour.

1. **Presentation** is with gradual-onset dimming of vision associated with shimmering photopsiae, bizarre visual images and acute-onset night-blindness (nyctalopia).
2. **Signs**
   - Progressive, bilateral, sometimes asymmetrical, visual loss, ring scotomas and colour vision abnormalities.
   - The fundus may appear normal or show arteriolar attenuation and occasionally optic atrophy (Fig. 13.114).
3. **ERG** is subnormal and may become extinguished.

Fig. 13.114
Arteriolar attenuation in cancer-associated retinopathy

4. **Treatment** options include systemic steroids, intravenous immunoglobulins and plasmapheresis but the prognosis is poor.

> ***NB:*** Melanoma-related retinopathy (MAR) is similar to but rarer than CAR and occurs in patients with established metastatic cutaneous melanomas.

Valsalva maculopathy

Valsalva maculopathy is a rare condition caused by transmission of sudden and severe increase in intrathoracic or intra-abdominal pressure to the eye resulting in intraocular bleeding.

1. **Signs.** Small, unilateral or bilateral, macular haemorrhages which are most frequently pre-retinal (Fig. 13.115).
2. **Prognosis** is excellent with spontaneous resolution without sequelae.

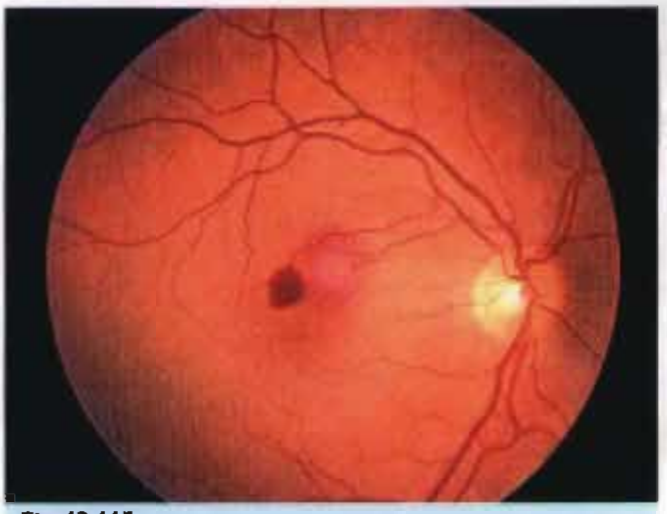


Fig. 13.115
Valsalva maculopathy

CHAPTER 14

Retinal Vascular Disease

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Diabetic retinopathy

Systemic considerations

Diabetes mellitus is a common metabolic disorder characterized by sustained hyperglycaemia of variable severity, secondary to lack, diminished efficacy, or both of endogenous insulin. Diabetes may be insulin-dependent (IDDM) or non-insulin-dependent (NIDDM), perhaps more accurately termed type 1 and type 2 diabetes respectively (*see* Chapter 20). Diabetic retinopathy (DR) is commoner in type 1 (40%) than in type 2 diabetes mellitus (20%), and is the most common cause of legal blindness between the ages of 20 and 65 years.

Risk factors

1. **Duration of diabetes** is the most important. In patients diagnosed with diabetes before the age of 30 years, the incidence of DR after 10 years is 50% and after 30 years 90%. DR rarely develops within 5 years of the onset of diabetes or before puberty, but about 5% of type 2 diabetics have DR at presentation.
2. **Poor metabolic control** is less important than duration, but is nevertheless relevant to the development and progression of DR.
3. **Pregnancy** is occasionally associated with rapid progression of DR. Predicating factors include poor pre-pregnancy control of diabetes, too rapid tightening of control during the early stages of pregnancy and the development of pre-eclampsia and fluid imbalance.
4. **Hypertension**, if poorly controlled, is associated with worsening of DR and the development of proliferative diabetic retinopathy (PDR) in both type 1 and type 2 diabetics.
5. **Nephropathy**, if severe, is associated with worsening of DR. Conversely, treatment of renal disease (e.g. renal transplantation) may be associated with improvement of retinopathy and a better response to photocoagulation.
6. **Other** risk factors include smoking, obesity and hyperlipidaemia.

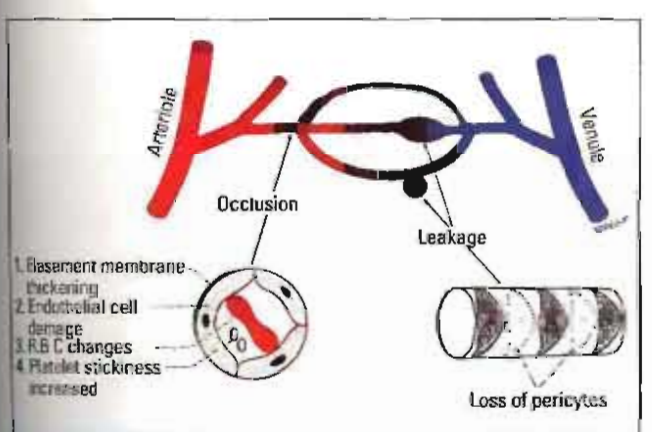


Fig. 14.1
Pathogenesis of diabetic retinopathy

Benefits of intensive metabolic control

- It delays the onset of DR, although it does not prevent it.
- It slows the progression of background diabetic retinopathy (BDR).
- It decreases the rate of conversion of pre-proliferative retinopathy (PPDR) to PDR.
- It decreases the incidence of macular oedema.
- It decreases the need for laser photocoagulation.

Pathogenesis

DR is a microangiopathy primarily affecting the pre-capillary arterioles, capillaries and post-capillary venules, although larger vessels may also be involved. Retinopathy exhibits features of both microvascular occlusion and leakage. Clinically, DR may be: (a) *background (non-proliferative)* in which the pathology remains intraretinal, (b) *proliferative* in which the pathology extends onto or beyond the retinal surface and (c) *pre-proliferative*, which has features of imminent proliferative disease.

Microvascular occlusion

1. **Pathogenesis** (Fig. 14.1)
   a. ***Capillary*** changes consist of loss of pericytes, thickening of the basement membrane and damage and proliferation of endothelial cells. Figure 14.2 shows a normal capillary bed and Figure 14.3 the capillary bed in a diabetic fundus.
   b. ***Haematological*** changes consist of deformation and increased rouleaux formation of red blood cells and increased platelet stickiness and aggregation, leading to decreased oxygen transport.
2. **The consequence** of retinal capillary non-perfusion is retinal ischaemia, which initially develops in the mid-retinal periphery. The two main effects of retinal hypoxia are the following (Fig. 14.4):

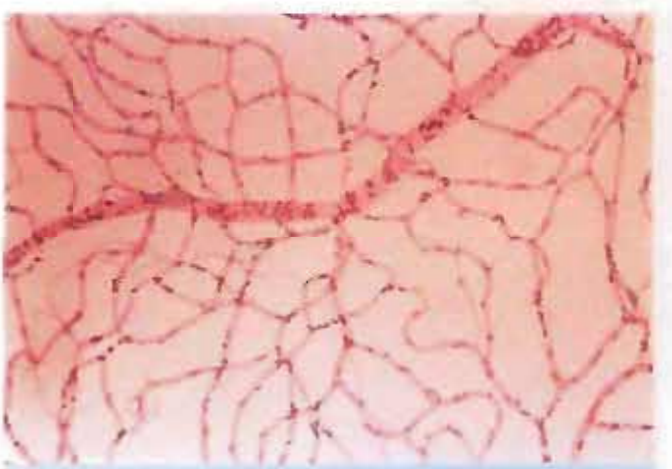


Fig. 14.2
Normal retinal capillary bed showing equal distribution between pericytes with round dark stained nuclei and endothelial cells with elongated pale staining cells

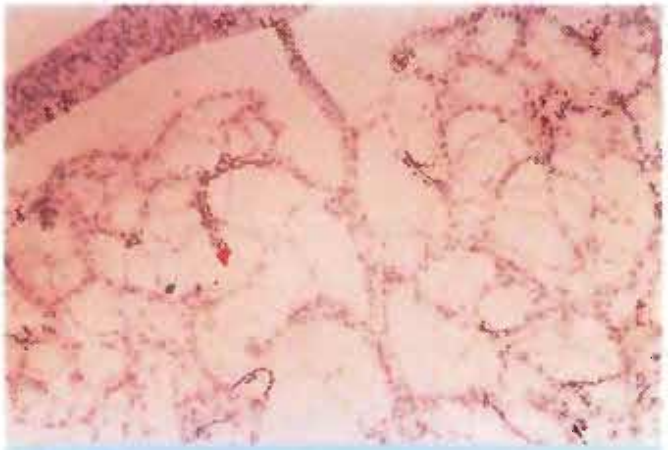


Fig. 14.3
Diabetic retinal capillary bed with many acellular capillaries due to occlusion; remaining capillaries are dilated and show loss of pericytes and an increased number of endothelial cells

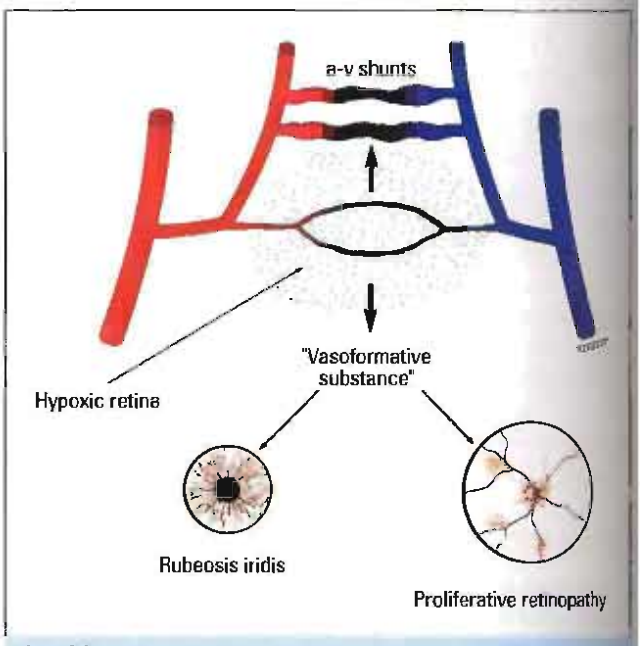


Fig. 14.4
Consequences of retinal ischaemia in diabetic retinopathy

a. ***Arteriovenous shunts*** associated with significant capillary occlusion ('drop-out') run from arterioles to venules. As it is unclear whether these lesions represent new vessels or opening of pre-existing vascular channels, they are often referred to as 'intraretinal microvascular abnormalities' (IRMA).

b. ***Neovascularization*** is thought to be caused by 'vasoformative substances' (growth factors) elaborated by hypoxic retinal tissue in an attempt to revascularize hypoxic retina. These substances promote neovascularization on the retina and optic nerve head (PDR) and occasionally on the iris (rubeosis iridis). Many growth factors have been identified: vascular endothelial growth factor (VEGF) appears to be of particular importance.

Microvascular leakage

1. **Pathogenesis**. Breakdown of the inner blood–retinal barrier leads to leakage of plasma constituents into the retina (Fig. 14.5b). Physical weakening of the capillary walls results in localized saccular outpouchings of the vessel wall, termed microaneurysms, which may leak or become thrombosed.
2. **Consequences** of increased vascular permeability include the development of intraretinal haemorrhages and oedema which may be diffuse or localized (Fig. 14.6).
   a. ***Diffuse retinal oedema*** is caused by extensive capillary dilatation and leakage.

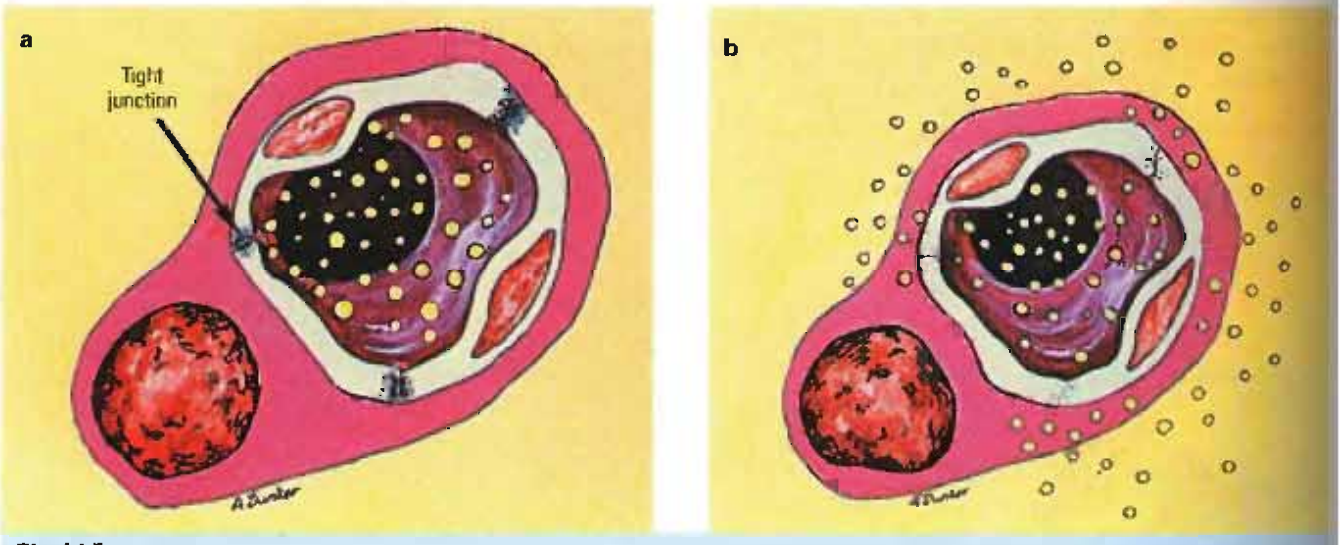


Fig. 14.5
(a) Tight junctions of endothelial cells forming the inner blood–retinal barrier; **(b)** leakage due to disruption of the inner blood–retinal barrier in diabetic retinopathy (Courtesy of Wilmer Institute)

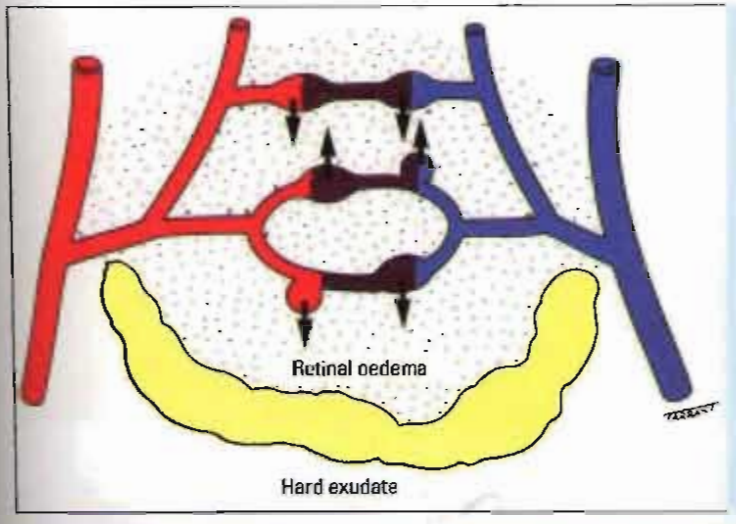


Fig. 14.6
Consequences of increased vascular permeability in diabetic retinopathy

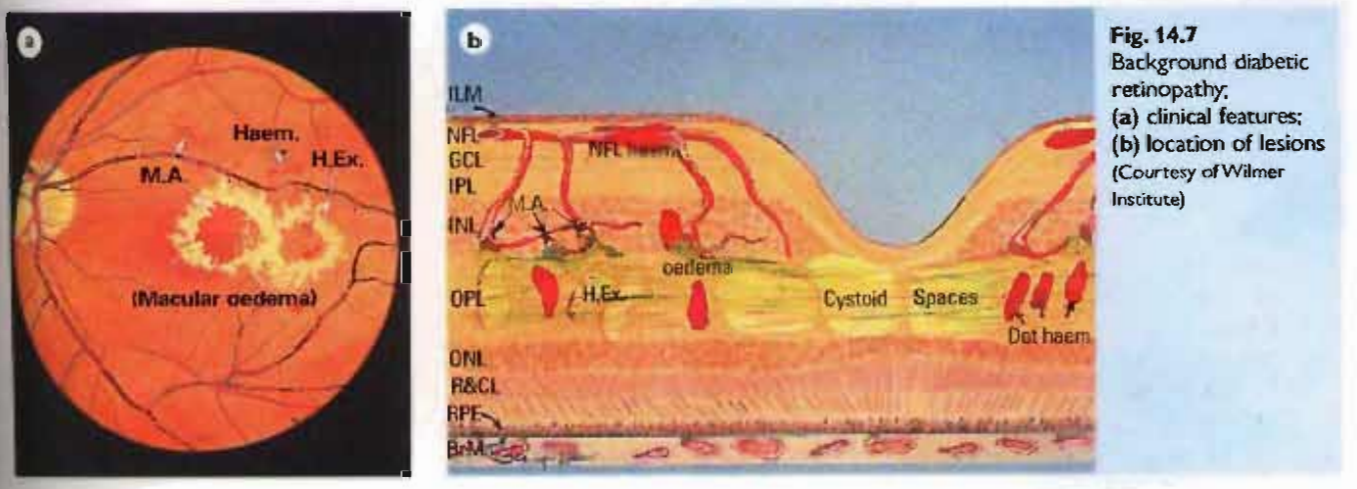


Fig. 14.7
Background diabetic retinopathy:
(a) clinical features;
(b) location of lesions
(Courtesy of Wilmer Institute)

b. Localized retinal oedema is caused by focal leakage from microaneurysms and dilated capillary segments. Chronic localized retinal oedema leads to the deposition of 'hard exudates' at the junction of normal and oedematous retina. These exudates, composed of lipoprotein and lipid-filled macrophages, typically surround leaking microvascular lesions in a circinate pattern. When leakage ceases, they absorb spontaneously over a period of months or years, either into the healthy surrounding capillaries or by phagocytosis of their lipid content. Chronic leakage leads to enlargement of the exudates and the deposition of cholesterol.

Background diabetic retinopathy

Clinical features

Figure 14.7a shows the clinical features of background DR and Figure 14.7b the location of the lesions within the retina.

1. **Microaneurysms** (Fig. 14.8) are located in the inner nuclear layer and are the earliest clinically detectable lesions.
   a. Signs. Tiny, round, red dots, initially appearing temporal to the fovea (Fig. 14.9). When coated with blood they may be indistinguishable from dot haemorrhages.
   b. FA shows tiny hyperfluorescent dots, representing non-thrombosed microaneurysms, typically in greater

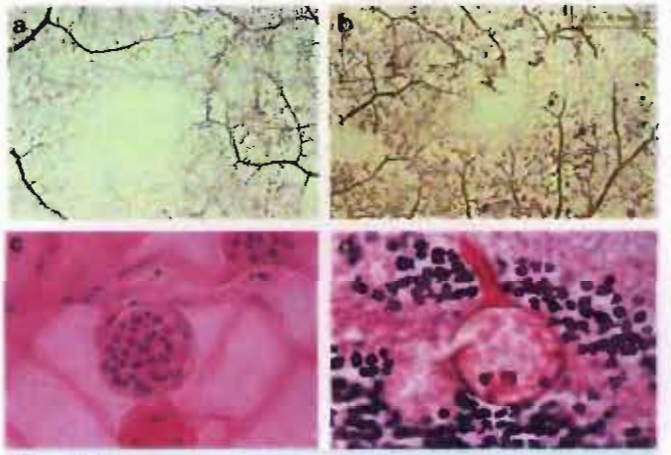


Fig. 14.8
(a) Trypsin digest of normal retina; (b) trypsin digest of diabetic retina showing perifoveal microaneurysms; (c) high power view showing a microaneurysm containing many cells; (d) cross-section of a microaneurysm (Courtesy of Wilmer Institute)

Fig. 14.9
Microaneurysms and dot haemorrhages in early background diabetic retinopathy

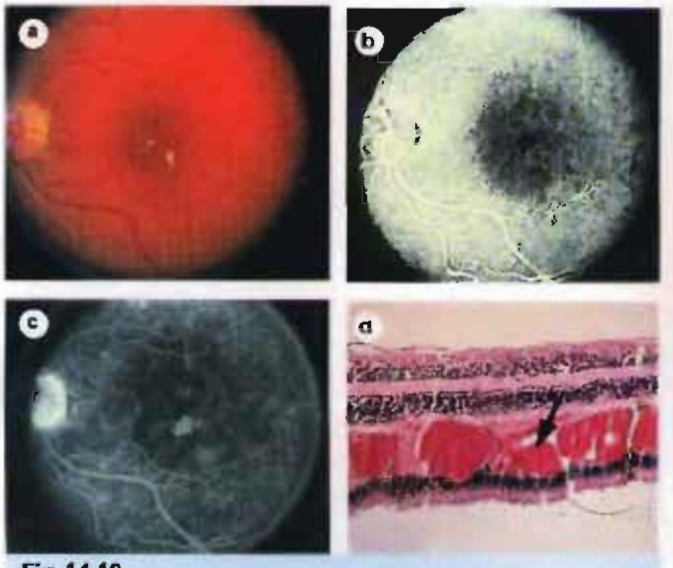


Fig. 14.10
Background diabetic retinopathy. **(a)** Hard exudates; **(b)** early FA showing microaneurysms; **(c)** late FA showing leakage; **(d)** hard exudate in the outer plexiform layer (Courtesy of Wilmer Institute)

numbers than that visible ophthalmoscopically (Fig. 14.10b). Late frames show diffuse hyperfluorescence due to leakage (Fig. 14.10c).

2. **Hard exudates** lie within the outer plexiform layer (Fig. 14.10d).
   a. Signs. Waxy, yellow lesions with relatively distinct margins (Fig. 14.10a) often arranged in clumps and/or rings at the posterior pole (Fig. 14.11). A ring of hard exudates (circinate exudate) often exhibits microaneurysms at its centre. With time, number and size tend to increase, and the fovea may be threatened or involved (Fig. 14.12).
   b. FA shows hypofluorescence due to blockage of background choroidal fluorescence.
3. **Retinal oedema** is initially located between the outer plexiform and inner nuclear layers. Later it may also involve the inner plexiform and nerve fibre layers, until eventually the entire thickness of the retina becomes oedematous. With further accumulation of fluid the fovea assumes a cystoid appearance (cystoid macular oedema) (*see* Fig. 13.82).
   a. Signs. Retinal thickening is best detected by slit-lamp biomicroscopy with a Goldmann lens.
   b. FA shows diffuse late hyperfluorescence due to retinal capillary leakage (*see* Fig. 14.10c).
4. **Haemorrhages**
   *a. **Intraretinal*** haemorrhages arise from the venous end of capillaries and are located in the compact middle layers of the retina with a resultant red, 'dot-blot' configuration (*see* Fig. 14.11).
   *b. **Retinal nerve fibre layer*** haemorrhages arise from the larger superficial pre-capillary arterioles and are therefore flame-shaped.

Fig. 14.11
Severe background diabetic retinopathy with circinate exudates and haemorrhages

Fig. 14.12
Hard exudates at the macula in background diabetic retinopathy

Management

Patients with mild BDR require no treatment but should be reviewed annually. Apart from optimal control of diabetes,

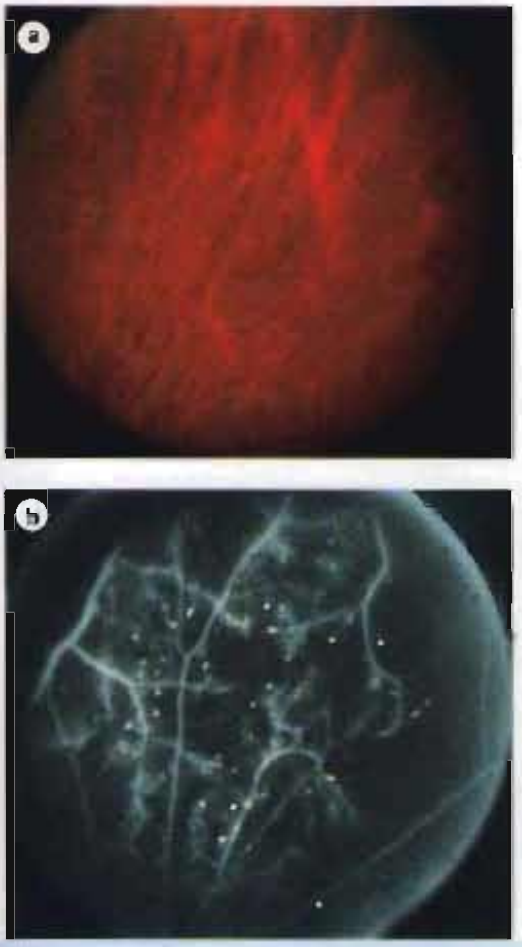


Fig. 14.13
(a) Peripheral retinal ischaemia; (b) FA showing capillary non-perfusion (Courtesy of Wilmer Institute)

associated factors such as hypertension, anaemia or renal failure should also be addressed.

Preproliferative diabetic retinopathy

BDR that exhibits signs of imminent proliferative disease is termed preproliferative diabetic retinopathy (PPDR). The clinical signs of PPDR indicate progressive retinal ischaemia, seen on FA as extensive hypofluorescent areas of retinal non-perfusion (capillary drop-out) (Fig. 14.13b). Figure 14.14a shows the clinical features of PPDR and Figure 14.14b the location of the lesions. The risk of progression to proliferative disease appears proportional to the number of lesions.

Clinical features

1. **Cotton wool spots** represent focal infarcts of the retinal nerve fibre layer, due to occlusion of pre-capillary arterioles (Fig. 14.15c and d). Interruption of axoplasmic transport with subsequent build-up of transported material within the axons (axoplasmic stasis) are responsible for the white appearance of the lesions.
   a. Signs. Small, whitish, fluffy superficial lesions which obscure underlying blood vessels and are clinically

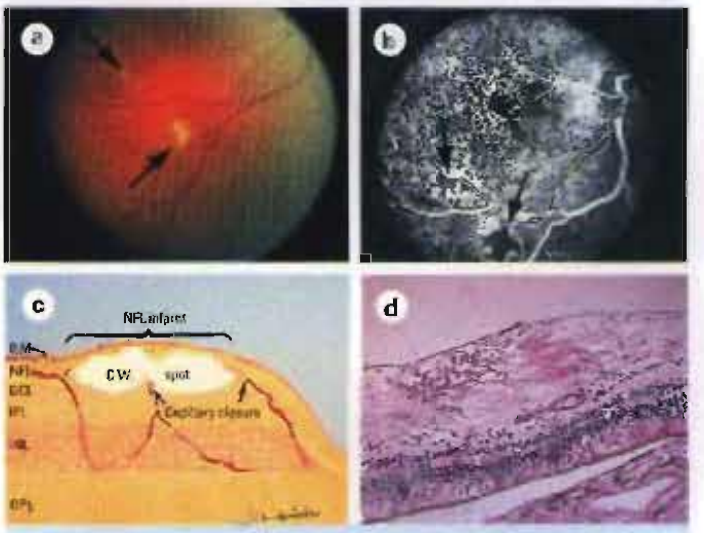


Fig. 14.15
(a) Cotton wool spots; (b) FA showing hypofluorescence due to blockage by the cotton wool spots and small adjacent areas of capillary non-perfusion; (c) cotton wool spot adjacent to an area of capillary closure; (d) low-power photomicrograph showing infarction and disorganization of the retinal nerve fibre layer and ganglion cell layer following capillary closure (Courtesy of Wilmer Institute)

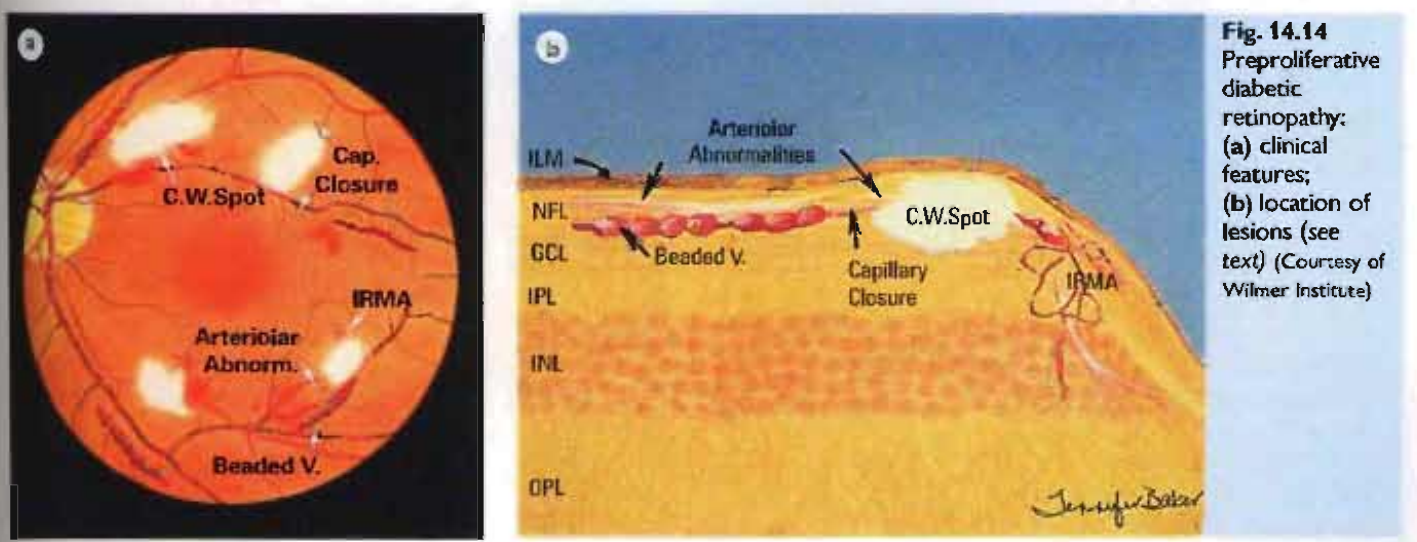


Fig. 14.14
Preproliferative diabetic retinopathy: (a) clinical features; (b) location of lesions (see *text*) (Courtesy of Wilmer Institute)

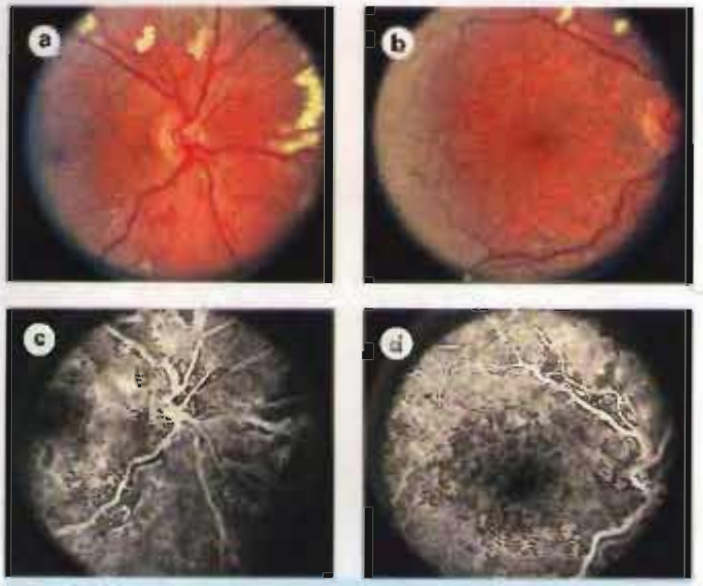


Fig. 14.16
(a and b) Cotton wool spots and venous dilatation; (c and d) FA showing spotty hyperfluorescence of microaneurysms and areas of hypofluorescence due to capillary non-perfusion
(Courtesy of Wilmer Institute)

evident only in the post-equatorial retina, where the nerve fibre layer is of sufficient thickness to render them visible (Figs 14.15a, and 14.16a and b).

b. FA shows focal hypofluorescence due to blockage of background choroidal fluorescence frequently associated with adjacent capillary non-perfusion (Figs 14.15b, and 14.16c and d).

2. **Intraretinal microvascular abnormalities (IRMA)** represent shunts that run from retinal arterioles to venules, thus by-passing the capillary bed, and are therefore often seen adjacent to areas of capillary closure (Fig. 14.17a).

a. Signs. Fine red lines that run from arterioles to venules, thus resembling focal areas of flat retinal new vessels (Figs 14.17b and 14.18a). The main distinguishing features of IRMA are their intraretinal location, their failure to cross major retinal blood vessels and absence of leakage on FA.

b. FA shows focal hyperfluorescence associated with adjacent areas of capillary closure (Fig. 14.18b).

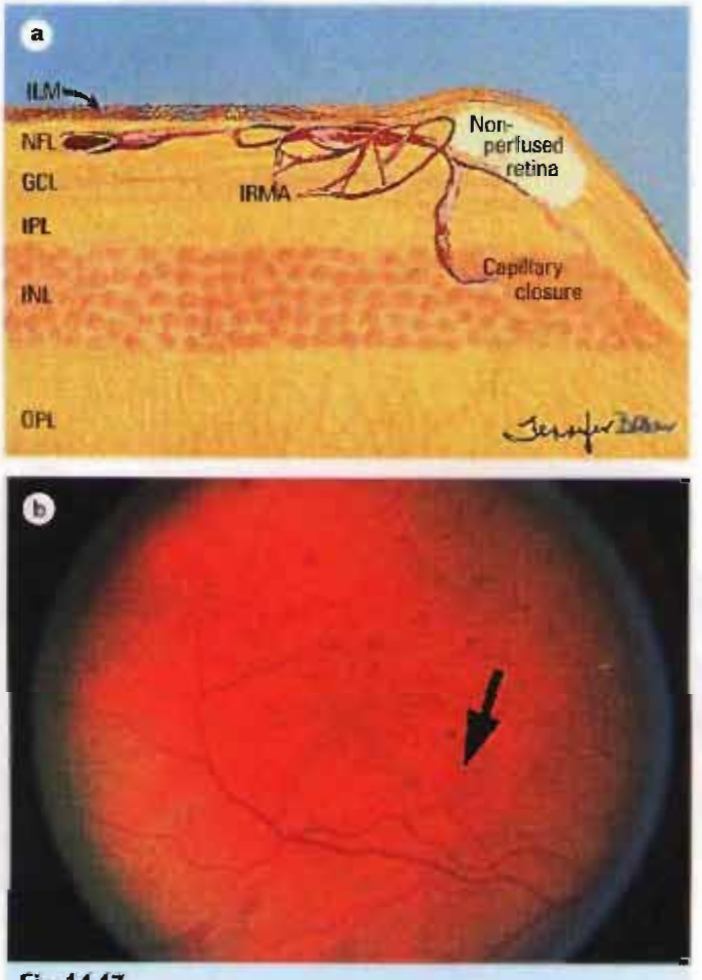


Fig. 14.17
Intraretinal microvascular abnormalities. (a) Location in the superficial retina adjacent to areas of non-perfusion; (b) clinical appearance (Courtesy of Wilmer Institute)

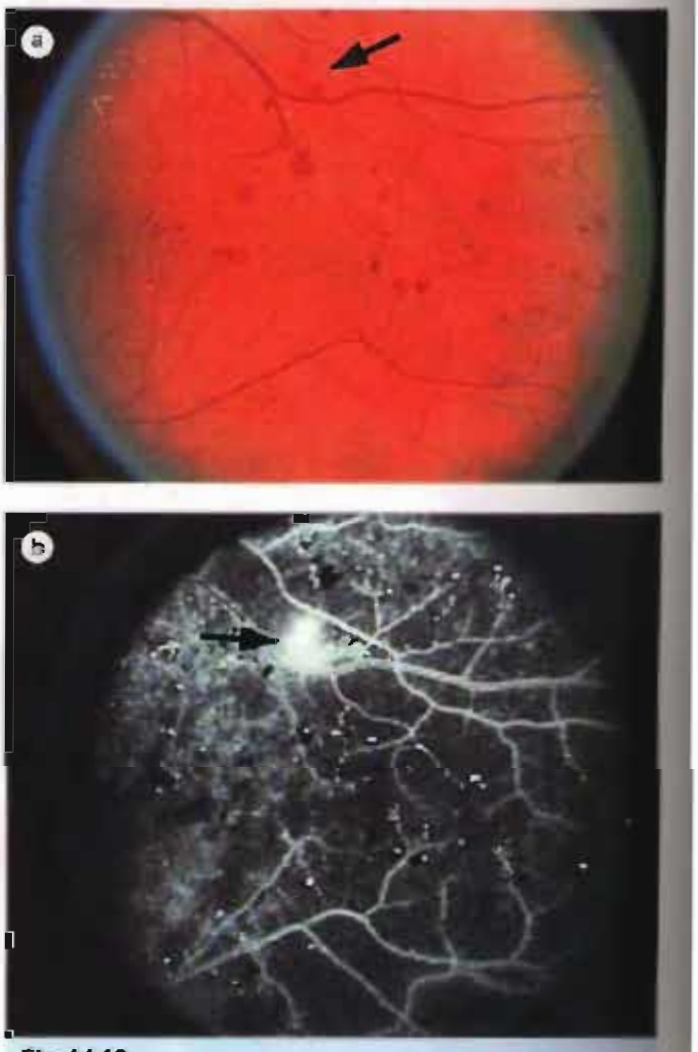


Fig. 14.18
(a) Intraretinal microvascular abnormalities; (b) FA showing focal hyperfluorescence and extensive capillary non-perfusion
(Courtesy of Wilmer Institute)

Fig. 14.19
Venous looping

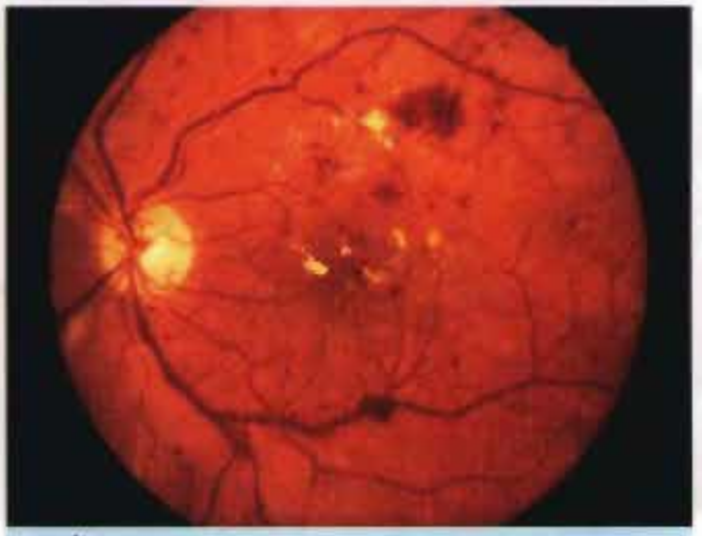


Fig. 14.22
Preproliferative diabetic retinopathy. Venous dilatation, looping and intraretinal microvascular abnormalities along the inferotemporal arcade, blot haemorrhages inside the superotemporal arcade and hard exudates at the macula

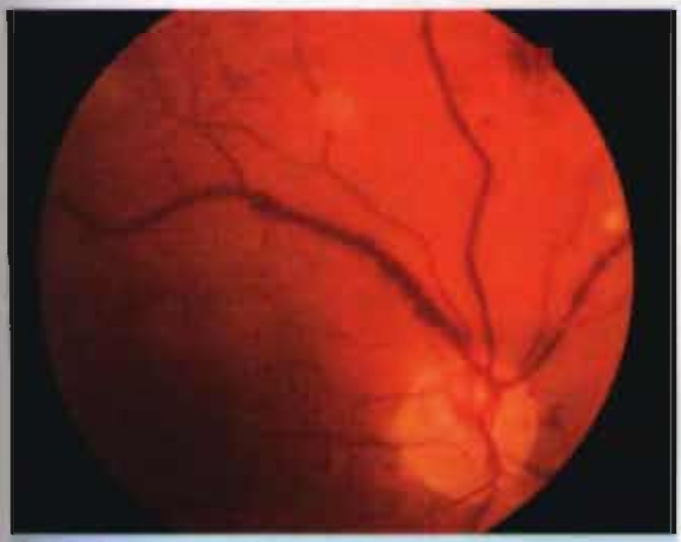


Fig. 14.20
Venous beading and [illegible] vessels

3. **Venous changes** consist of dilatation (*see* Fig. 14.16a and b), looping (Fig. 14.19), beading (Fig. 14.20) and 'sausage-like' segmentation.
4. **Arterial changes** consisting of narrowing, silver-wiring and obliteration resembling a branch retinal artery occlusion (Fig. 14.21).
5. **Dark blot haemorrhages** (Fig. 14.22) represent haemorrhagic retinal infarcts and are located within the middle retinal layers.

Management

PPDR should be watched closely because of the risk of PDR. Treatment by photocoagulation is usually not appropriate unless regular follow-up is not possible, or vision in the fellow eye has been already lost due to proliferative disease.

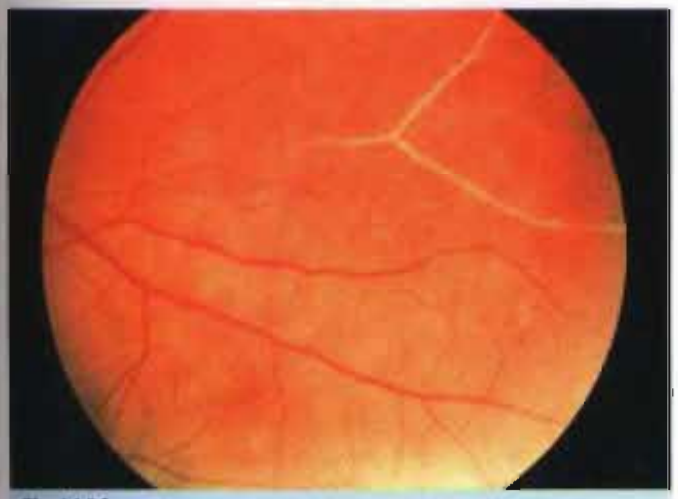


Fig. 14.21
Peripheral arteriolar occlusion

Diabetic maculopathy

Involvement of the fovea by oedema and hard exudates or ischaemia (diabetic maculopathy) is the most common cause of visual impairment in diabetic patients, particularly those with type 2 diabetes.

Classification

1. **Focal exudative**
   - *a. Signs.* Well-circumscribed retinal thickening associated with complete or incomplete rings of perifoveal hard exudates (Fig. 14.23b).
   - *b. FA* shows late, focal hyperfluorescence due to leakage and good macular perfusion (Fig. 14.23c).
2. **Diffuse exudative**
   - *a. Signs.* Diffuse retinal thickening, which may be associated with cystoid changes. Obliteration of landmarks

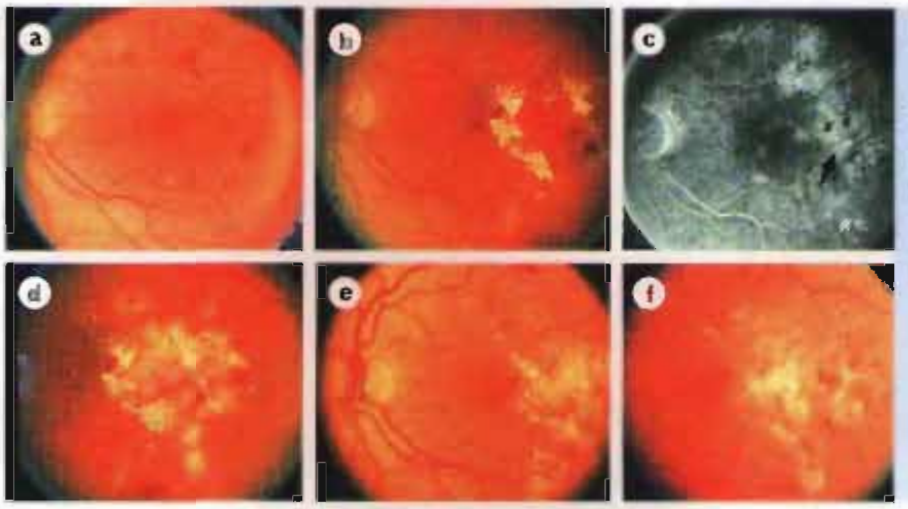


Fig. 14.23
Focal diabetic maculopathy. (a) Initial appearance showing only haemorrhages; (b) 2 years later showing a ring of hard exudates; (c) FA shows corresponding focal leakage; (d) appearance immediately following focal laser photocoagulation; (e) resolving hard exudates; (f) complete resolution of hard exudates and residual laser scars several months later (Courtesy of Wilmer Institute)

by severe oedema may render localization of the fovea impossible (Fig. 14.24a).

b. FA shows widespread spotty hyperfluorescence of microaneurysms (Fig. 14.24b) and late diffuse hyperfluorescence due to leakage, which is frequently more dramatic than on clinical examination, with a flower-petal pattern if CMO is present (Fig. 14.24c).

3. Ischaemic

a. Signs. Reduced visual acuity in association with a relatively normal appearance of the fovea (Fig. 14.25a). Associated PPDR is frequent. Dark blot haemorrhages may be seen.

b. FA shows capillary non-perfusion at the fovea (Fig. 14.25b), the severity of which does not always relate to the level of visual acuity. Other areas of capillary non-perfusion are also frequently present at the posterior pole and periphery.

4. Mixed is characterized by features of both ischaemia and exudation.

Clinically significant macular oedema

Definition

Clinically significant macular oedema (CSMO) has the following characteristics.

Fig. 14.24
Diffuse diabetic maculopathy. (a) A few hard exudates and dot haemorrhages; (b) early FA phase showing spotty hyperfluorescence of microaneurysms; (c) later phase FA showing extensive leakage and cystoid macular oedema (Courtesy of Wilmer Institute)

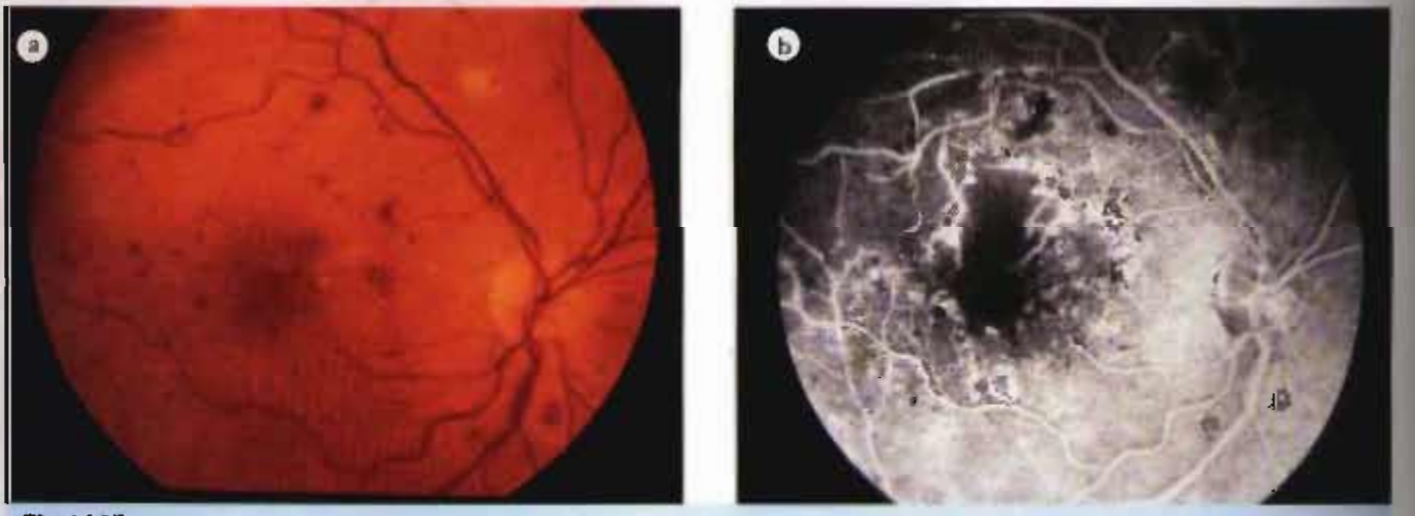


Fig. 14.25
Ischaemic diabetic maculopathy. (a) Dot and blot haemorrhages; (b) FA showing macular and peripheral non-perfusion

- Retinal oedema within 500 μm of the centre of the fovea (Fig. 14.26a).
- Hard exudates within 500 μm of the centre of the fovea, if associated with adjacent retinal thickening (which may be outside the 500 μm limit) (Fig. 14.26b).
- Retinal oedema one disc area (1500 μm) or larger, any part of which is within one disc diameter of the centre of the fovea (Fig. 14.26c).

NB: CSMO requires laser photocoagulation irrespective of the level of visual acuity because treatment reduces the risk of visual loss by 50%. Improvement of visual function is infrequent, rendering such treatment prophylactic. Pre-treatment FA is useful to delineate the area and extent of leakage and also to detect capillary non-perfusion at the fovea (ischaemic maculopathy) which carries a poor prognosis and is a contraindication to treatment.

Argon laser photocoagulation

1. Technique

a. Focal treatment involves applying laser burns to microaneurysms and microvascular lesions in the centre of rings of hard exudates located 500–3000 μm from the centre of the fovea (*see* Fig. 14.23d). The spot size is 50–100 μm with a duration of 0.10 seconds and sufficient power to obtain gentle whitening or darkening of the microaneurysm. Treatment of lesions up to 300 μm from the centre of the fovea may be considered if CSMO persists despite previous treatment and visual acuity is less than 6/12. In these cases a shorter exposure time of 0.05 seconds is recommended.

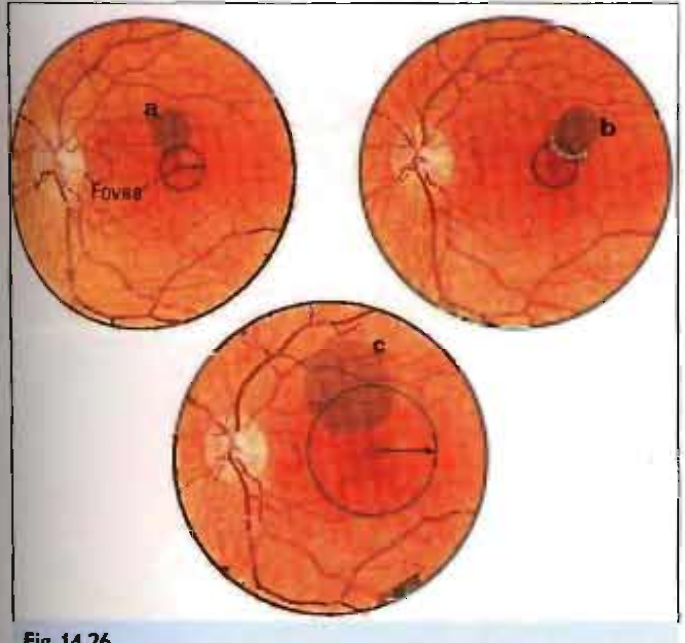


Fig. 14.26
Clinically significant macular oedema (see text)

b. Grid treatment is used for areas of diffuse retinal thickening located more than 500 μm from the centre of the fovea and 500 μm from the temporal margin of the optic disc. The spot size is 100–200 μm and exposure time 0.10 seconds. The burns should be of very light intensity and one burn-width apart.

2. Results. Approximately 70% of eyes achieve stable visual acuity. 15% show improvement and 15% subsequently deteriorate. Since it may take up to 4 months for the oedema to resolve (*see* Fig. 14.23f), re-treatment should not be considered prematurely.

3. Poor prognostic factors include:
- Hard exudates involving the fovea.
- Diffuse macular oedema.
- Cystoid macular oedema.
- Mixed exudative–ischaemic maculopathy.
- Severe retinopathy at presentation.

Vitrectomy

Pars plana vitrectomy may be indicated when macular oedema is associated with tangential traction from a thickened and taut posterior hyaloid membrane. In these cases laser therapy is of limited benefit but surgical release of tangential macular traction may be beneficial.

Proliferative diabetic retinopathy

PDR affects 5–10% of the diabetic population. Type 1 diabetics are at particular risk with an incidence of about 60% after 30 years. Protective factors include carotid occlusive disease, posterior vitreous separation, high myopia and optic atrophy.

Clinical features

1. Signs. Neovascularization is the hallmark of PDR. New vessels may proliferate on or within one disc diameter of the optic nerve head (NVD = new vessels at disc), or along the course of the major vessels (NVE = new vessels elsewhere), or both (Fig. 14.27a). It has been estimated that over one-quarter of the retina has to be non-perfused before PDR develops. The absence of the internal limiting membrane (ILM) at the optic nerve head may partially explain the predilection for neovascularization at this site. New vessels start as endothelial proliferations, arising most frequently from veins; they then pass through defects in the ILM to lie in the potential plane between the retina and posterior vitreous cortex, using the latter as a 'scaffold' for their growth (Fig. 14.27b).

2. FA, although not required to make the diagnosis (Fig. 14.28a), highlights the neovascularization during the early phases of the angiogram and shows hyperfluorescence during the later stages due to intense leakage of dye from neovascular tissue (Fig. 14.28b).

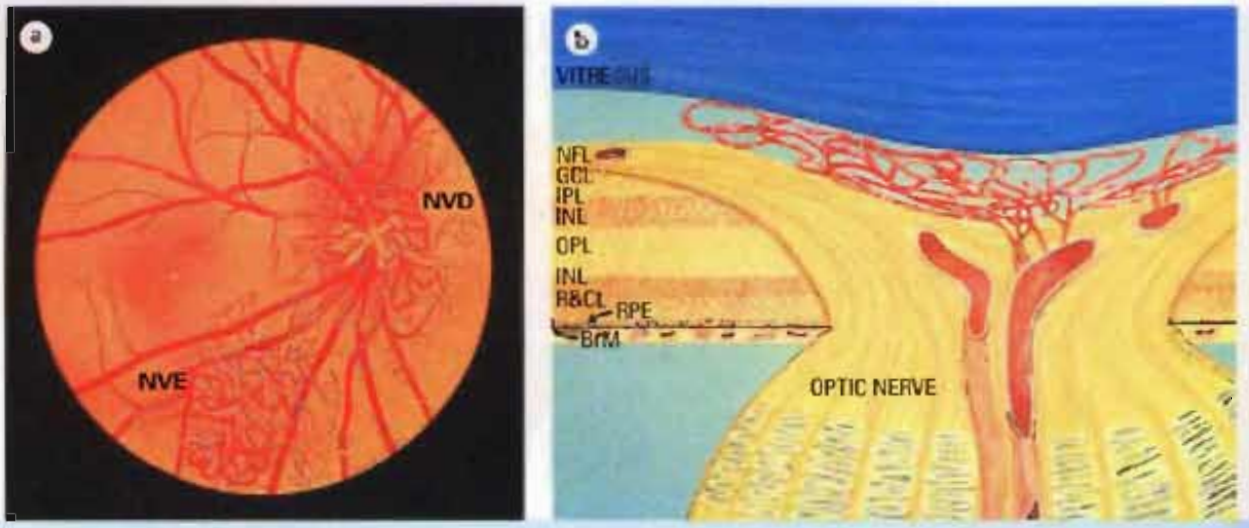


Fig. 14.27
Proliferative diabetic retinopathy. (a) Clinical features; (b) location of neovascularization (Courtesy of Wilmer Institute)

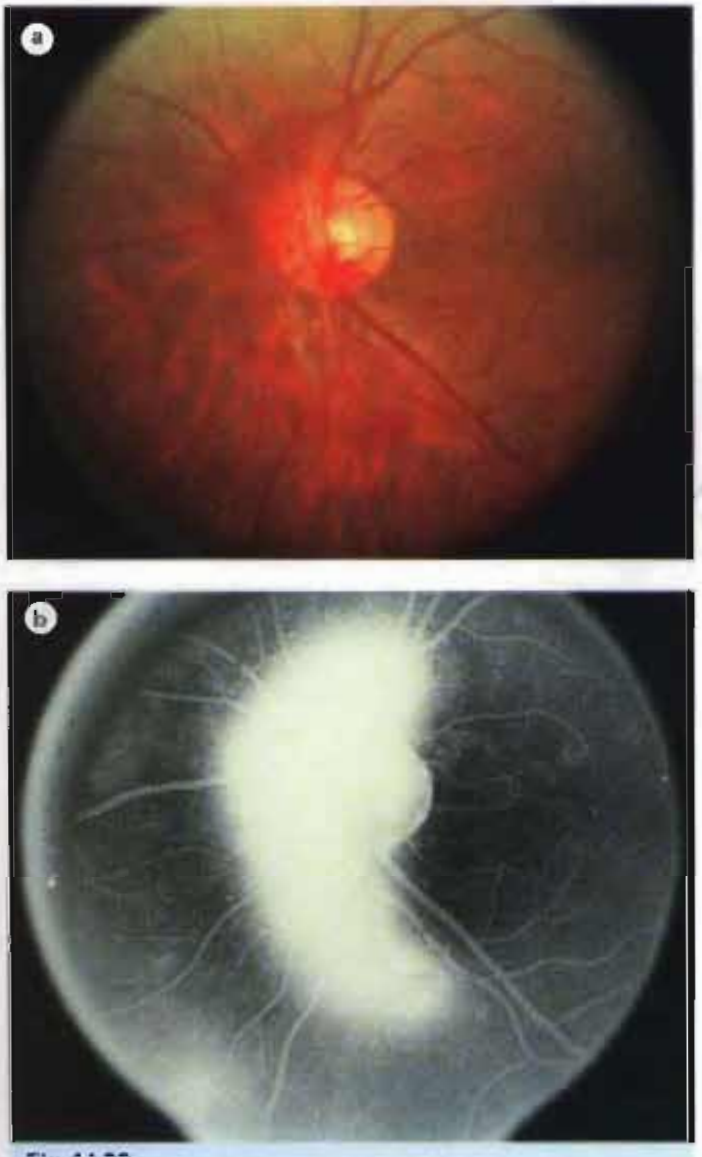


Fig. 14.28
(a) Disc new vessels; (b) late-phase FA shows extensive leakage (Courtesy of Wilmer Institute)

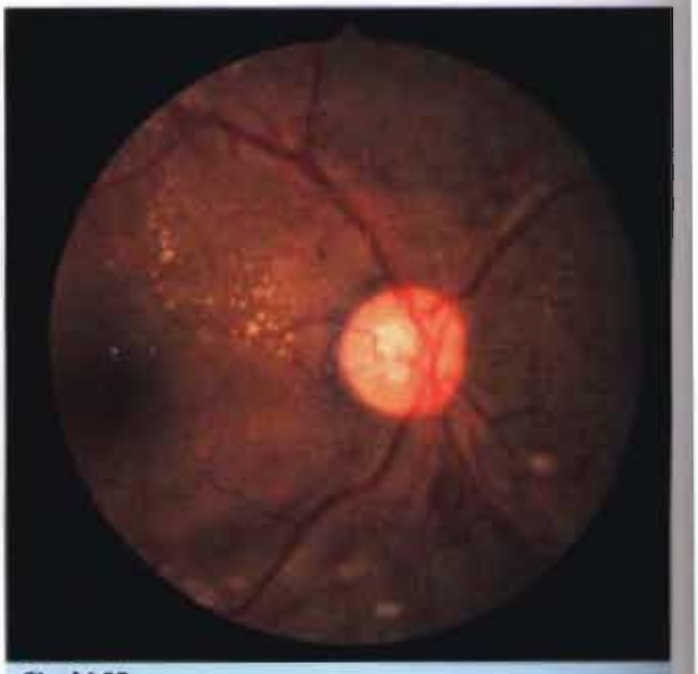


Fig. 14.29
Mild disc new vessels associated with severe preproliferative changes

Clinical assessment

1. **Severity** of PDR is determined by the area covered with new vessels in comparison with the area of the disc. The severity of PDR is described as follows:
   a. NVD
   - Mild when less than one-third disc area in extent (Fig. 14.29).
   - Severe when more than one-third disc area in extent (Fig. 14.30).

   b. NVE
   - Mild if less than half disc area in extent (Fig. 14.31a).
   - Severe if half disc area or more in extent (Fig. 14.31).

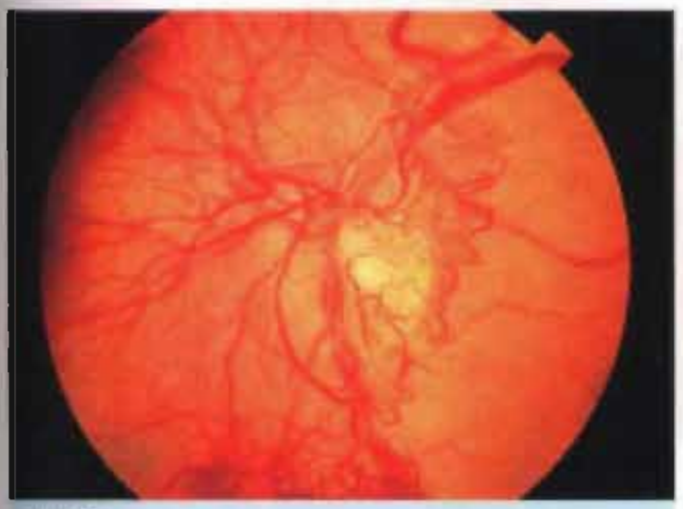


Fig. 14.30
Very severe disc new vessels

Fig. 14.32
Severe new vessels elsewhere

2. **Elevated** new vessels (Fig. 14.33 and *see* Fig. 14.31b–d) are less responsive to laser therapy than flat new vessels.
3. **Fibrosis** associated with neovascularization is important, since significant fibrous proliferation (Fig. 14.34), although less likely to bleed, carries an increased risk of tractional retinal detachment.
4. **Haemorrhage** which may be preretinal (subhyaloid) (Fig. 14.35) and/or intragel vitreous is an important risk factor for visual loss.
5. **High risk characteristics**. The following signify a high risk of severe visual loss within 2 years, if left untreated:
   - Mild NVD with haemorrhage (*see* Fig. 14.35a) carries a 26% risk of visual loss, which is reduced to 4% with treatment (*see* Fig. 14.35b).
   - Severe NVD without haemorrhage (*see* Fig. 14.30) carries a 26% risk of visual loss, which is reduced to 9% with treatment.
   - Severe NVD with haemorrhage (Fig. 14.36b) carries a 37% risk of visual loss, which is reduced to 20% with treatment (Fig. 14.36c and d).
   - Severe NVE with haemorrhage carries a 30% risk of visual loss, which is reduced to 7% with treatment.

NB: Unless the above criteria apply, it is recommended that photocoagulation be withheld and the patient be followed up at 3-monthly intervals. In practice, however, most ophthalmologists perform laser photocoagulation at the first sign of neovascularization.

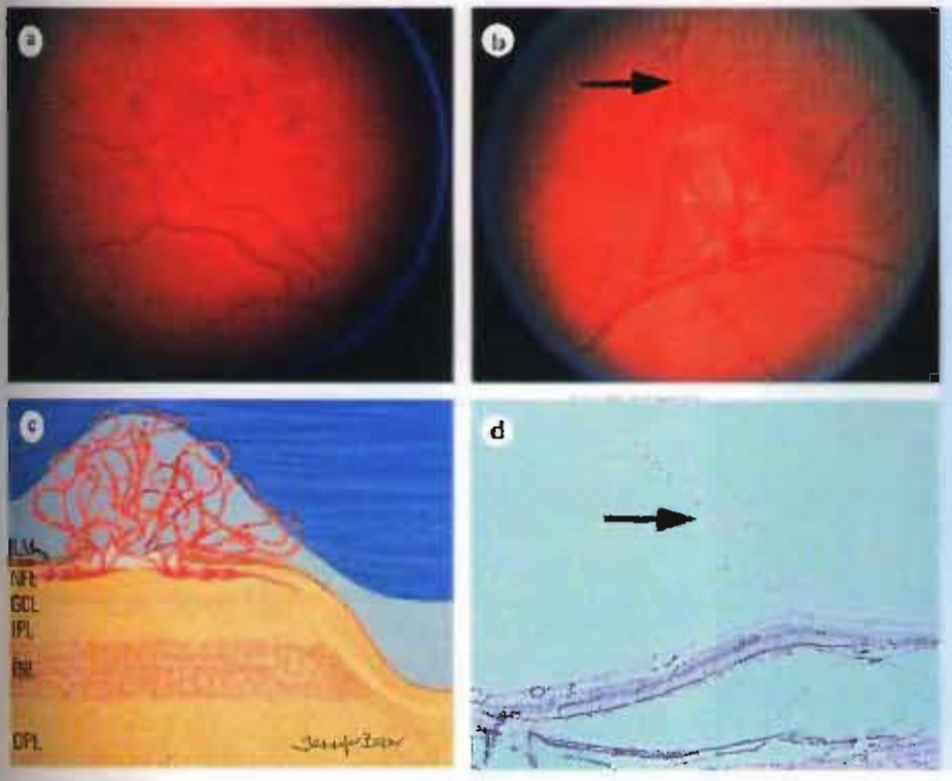


Fig. 14.31
Proliferative diabetic retinopathy; (a) flat new vessels elsewhere without fibrosis; (b) elevated new vessels elsewhere with fibrosis; (c) elevated new vessels elsewhere with partial vitreous separation; (d) histological section showing elevated new vessels elsewhere (Courtesy of Wilmer Institute)

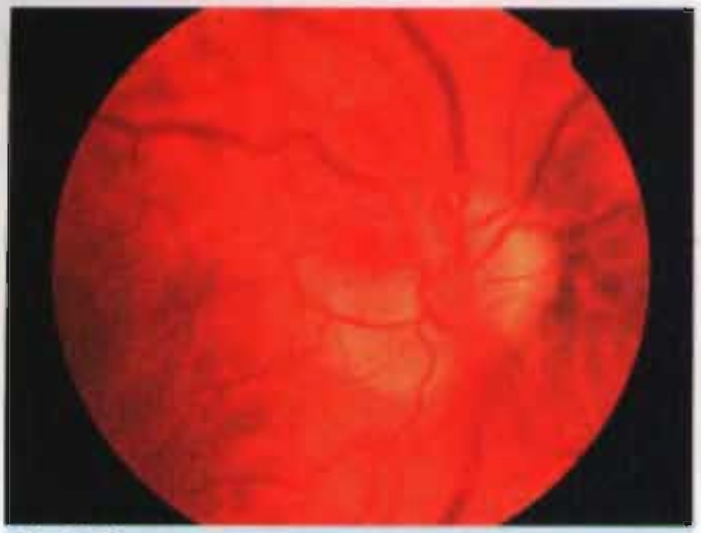
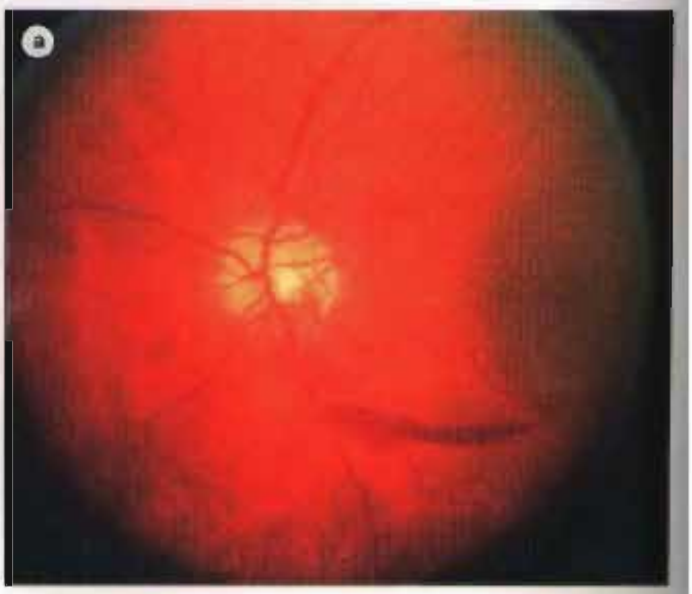


Fig. 14.33
Severe elevated disc new vessels



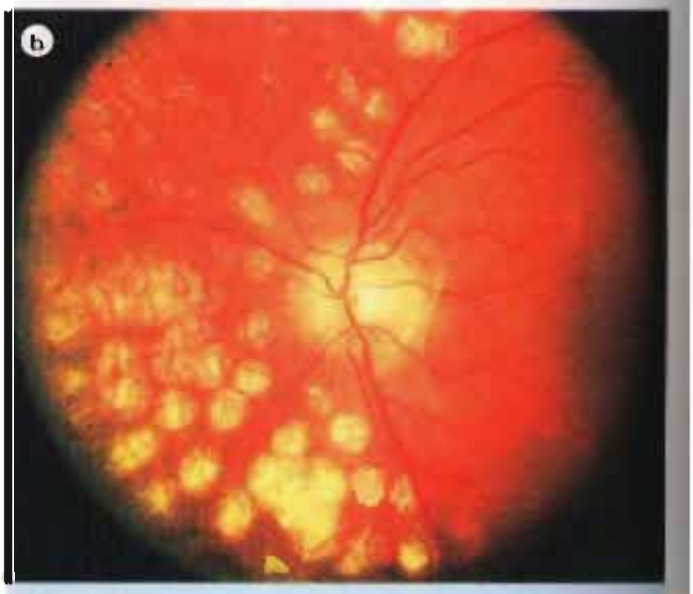


Fig. 14.35
Proliferative diabetic retinopathy (a); mild disc new vessels with preretinal haemorrhage; (b) involution following laser panretinal photocoagulation (Courtesy of Wilmer Institute)

Panretinal laser photocoagulation (PRP)

Laser therapy is aimed at inducing involution of new vessels and preventing visual loss from vitreous haemorrhage and tractional retinal detachment. The extent of treatment is dependent on the severity of PDR. Laser burns are placed further apart with less intensity (Fig. 14.37a and b) for mild disease and closer together and with greater intensity (Fig. 14.37c and d) for severe or recurrent disease.

> ***NB:*** In the beginner's hands, a panfundoscopic lens is perhaps safer than the Goldmann three-mirror lens, since it is relatively easy to inadvertently photocoagulate the posterior pole through the latter, with disastrous consequences.

1. Laser settings

a. Spot size depends on the contact lens used. With the Goldmann lens, spot size is set at 500 µm, but with a panfundoscopic lens it is set at 300–200 µm because of induced magnification.

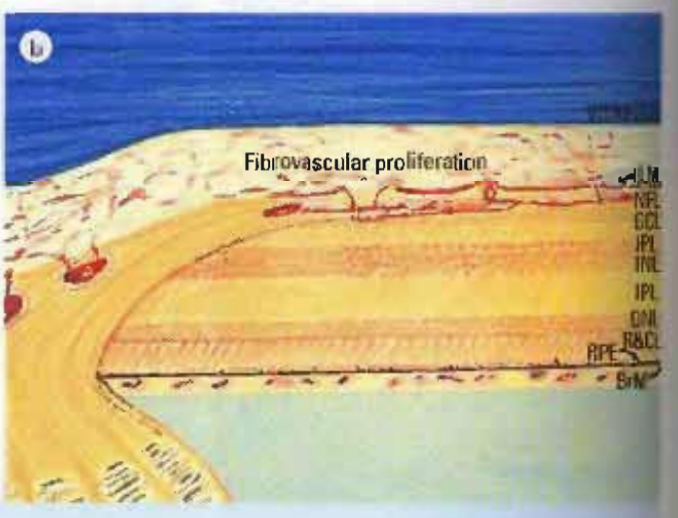


Fig. 14.34
Proliferative diabetic retinopathy (a); fibrovascular proliferation; (b) location between the internal limiting membrane and vitreous gel
(Courtesy of Wilmer Institute)

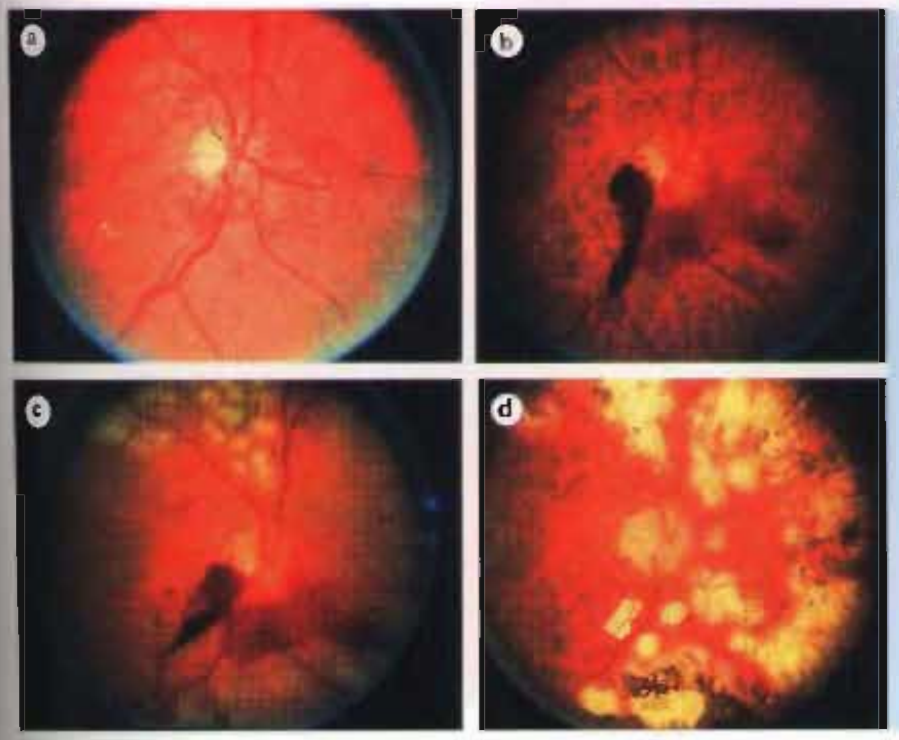


Fig. 14.36
Proliferative diabetic retinopathy: (a) severe disc new vessels; (b) preretinal and vitreous haemorrhage a few days later; (c) appearance immediately following laser panretinal photocoagulation; (d) appearance 3 months later showing involution of new vessels and heavy laser scars (Courtesy of Wilmer Institute)

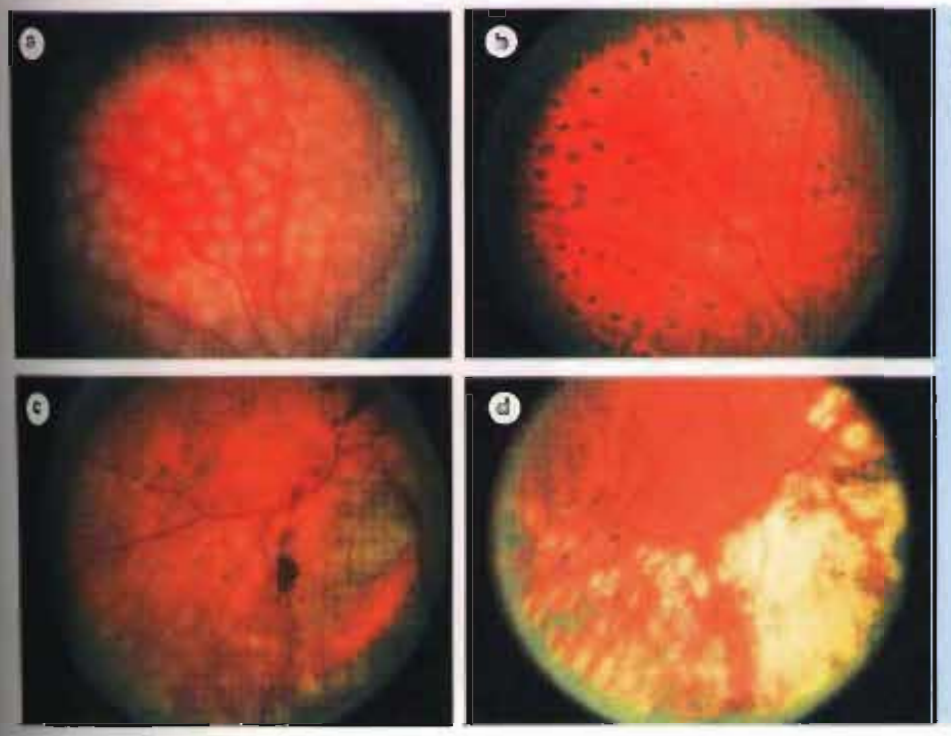


Fig. 14.37
Laser panretinal photocoagulation. (a and b) Standard; (c and d) intensive (Courtesy of Wilmer Institute)

b. *Duration* of the burn is 0.05–0.10 seconds at a power level that produces a gentle burn.

2. **Initial treatment** involves 2000–3000 burns in a scatter pattern, extending from the posterior fundus to cover the peripheral retina in one or more sessions. PRP completed in a single session carries a slightly higher risk of complications. The amount of treatment during any one session is governed by the patient's pain threshold and ability to maintain concentration. Topical corneal anaesthesia is adequate in most patients, although peribulbar or

3. **Sequence** is as follows:
   - *Step 1*. Close to the disc (Fig. 14.38a); below the inferior temporal arcades (Fig. 14.38b).
   - *Step 2*. Protective barrier around the macula (Fig. 14.39a) to prevent inadvertent treatment of the fovea; above the superotemporal arcade (Fig. 14.39b).
   - *Step 3*. Nasal to the disc (Fig. 14.40a); completion of posterior pole treatment (Fig. 14.40b).
   - *Step 4*. Peripheral treatment (Fig. 14.41a) until completion (Fig. 14.41b).

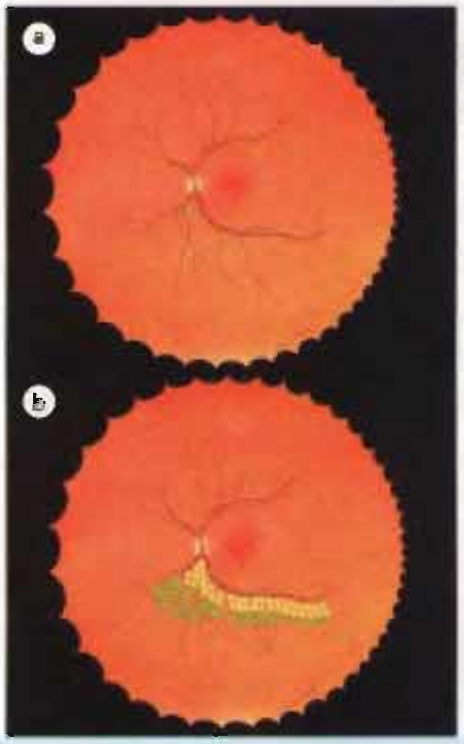


Fig. 14.38
Panretinal photocoagulation: step 1 (see *text*) (Courtesy of Wilmer Institute)

Fig. 14.39
Panretinal photocoagulation: step 2 (see *text*) (Courtesy of Wilmer Institute)

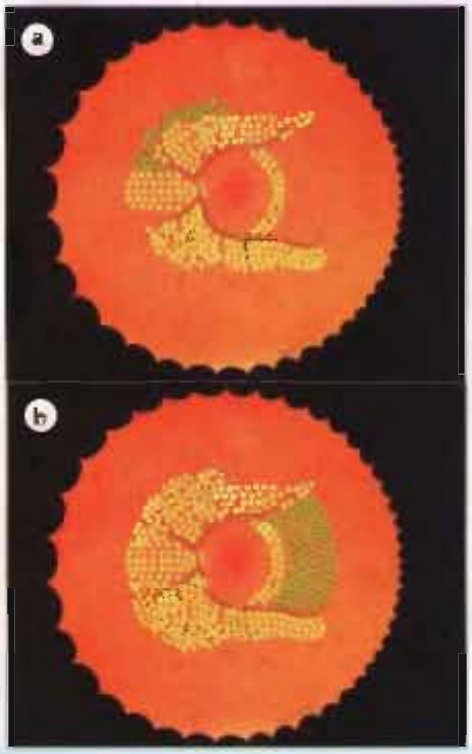


Fig. 14.40
Panretinal photocoagulation: step 3 (see *text*) (Courtesy of Wilmer Institute)

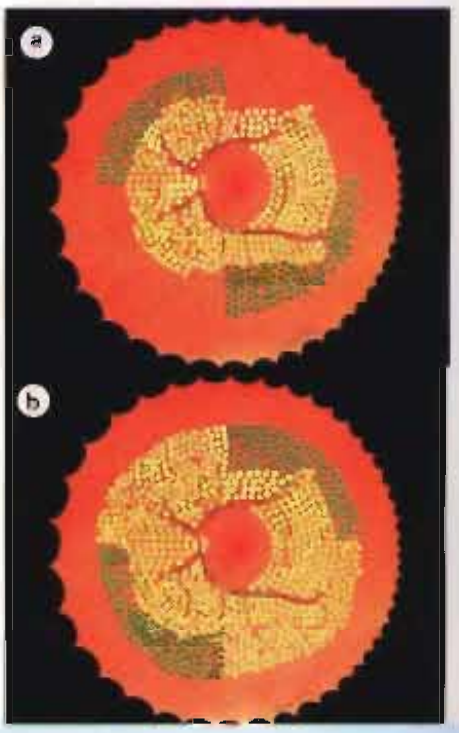


Fig. 14.41
Panretinal photocoagulation: step 4 (see *text*) (Courtesy of Wilmer Institute)

NB: In very severe PDR it is advisable to treat the inferior fundus first, since any vitreous haemorrhage will gravitate inferiorly and obscure this area, precluding further treatment.

Subsequent management

1. **Follow-up** is after 4–6 weeks. In eyes with severe NVD, several treatment sessions totalling 5000 or even more burns may be required, although complete elimination of

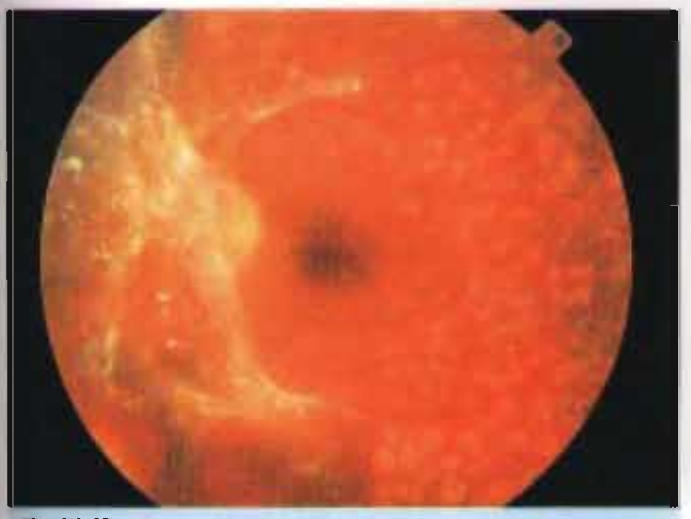


Fig. 14.42
Residual glial tissue following panretinal photocoagulation
(Courtesy of S. Milewski)

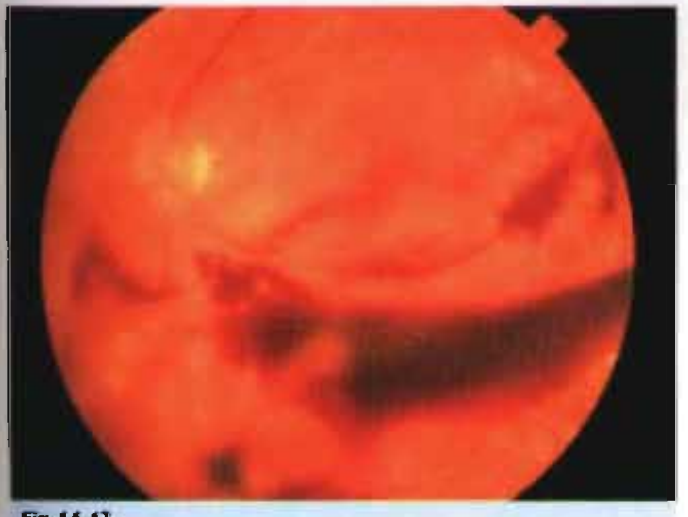


Fig. 14.43
Preretinal and intragel haemorrhage

NVD may be difficult and early vitreous surgery may be necessary. The most important cause of persistent neovascularization is inadequate treatment.

2. **Signs of involution** are regression of neovascularization leaving only 'ghost' vessels or fibrous tissue (*see* Fig. 14.35b), decrease in venous dilatation, absorption of retinal haemorrhages and disc pallor (*see* Fig. 14.36d). In most eyes, once the retinopathy is quiescent, stable vision is maintained. In a few eyes, recurrences of PDR occur despite an initial satisfactory response. It is therefore necessary to re-examine the patient at intervals of approximately 6–12 months.

NB: PRP influences only the vascular component of the fibrovascular process. Eyes in which new vessels have regressed leaving only fibrous tissue (Fig. 14.42) should not be re-treated.

3. **Treatment of recurrence**
   a. Further laser photocoagulation, filling in any gaps between previous laser scars.
   b. Cryotherapy to the anterior retina is particularly useful when further photocoagulation is impossible as a result of inadequate visualization of the fundus caused by opaque media. It also offers a means of treating areas of the retina spared by PRP.

NB: It should be explained to patients that PRP may result in visual field defects of sufficient severity to legally preclude driving a motor vehicle.

Advanced diabetic eye disease

Serious vision-threatening complications of diabetic retinopathy (advanced diabetic eye disease) occur in patients who have not had laser therapy or in whom laser photocoagulation has been unsuccessful or inadequate. One or more of the following complications may occur.

Haemorrhage

This may occur into the vitreous gel, the retrohyaloid space (preretinal haemorrhage) or both (Fig. 14.43). A preretinal haemorrhage has a crescentic shape which demarcates the level of posterior vitreous detachment. Occasionally, a preretinal haemorrhage may penetrate the vitreous gel. Intragel haemorrhages usually take longer to clear than preretinal haemorrhages. In some eyes, altered blood becomes compacted on the posterior vitreous face to form an 'ochre membrane'. Patients should be warned that bleeding may be precipitated by severe physical exertion or straining, hypoglycaemia and direct ocular trauma. However, not infrequently bleeding occurs while the patient is asleep.

Tractional retinal detachment

This is caused by progressive contraction of fibrovascular membranes over large areas of vitreoretinal adhesion. Posterior vitreous detachment in diabetic eyes is gradual and, due to the strong adhesions of cortical vitreous to areas of fibrovascular proliferation, is usually incomplete.

1. **Pathogenesis**. The following types of static vitreoretinal traction may result in retinal detachment:
   a. Anteroposterior traction due to contraction of fibrovascular membranes extending from the posterior retina, usually in association with the major vascular arcades, to the vitreous base anteriorly (Fig. 14.44).
   b. Bridging (trampoline) traction is the result of contraction of fibrovascular membranes stretching from one part of the posterior retina to another (Fig. 14.45). This tends to pull the two involved points together and may result in the formation of stress lines as well as displacement of the macula towards the disc or elsewhere, depending on the direction of the tractional force.
2. **Signs** (*see* Chapter 12).

Other complications

1. **Opaque membranes** may develop on the posterior surface of the detached hyaloid and stretch from the superior to the

Fig. 14.44
Anteroposterior traction resulting in elevation of fibrovascular tissue

inferior temporal arcades (Fig. 14.46). Such membranes may obscure the macula and further impair visual acuity.

2. **Rubeosis iridis** (iris neovascularization) may occur in eyes with PDR, and if severe may lead to neovascular glaucoma (*see* Chapter 9). Rubeosis is particularly common in eyes with severe retinal ischaemia or persistent retinal detachment following unsuccessful pars plana vitrectomy.

Pars plana vitrectomy

This is the main method of treating severe complications of PDR.

1. Indications

a. Severe persistent vitreous haemorrhage is the most common indication. In these cases the density of the haemorrhage precludes adequate PRP. In the absence of rubeosis iridis, vitrectomy within 3 months of the initial vitreous haemorrhage should be considered in type 1 diabetics and at about 6 months in type 2 diabetics.

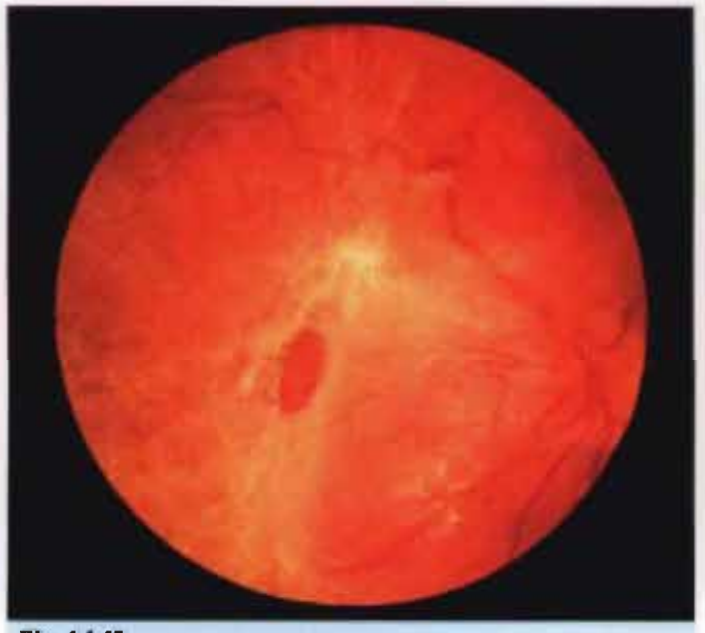


Fig. 14.45
Bridging traction resulting in contraction of fibrovascular tissue between the temporal arcades

Fig. 14.46
Extensive avascular glial tissue and a localized inferior tractional retinal detachment in inactive proliferative diabetic retinopathy (Courtesy of Wilmer Institute)

b. Tractional RD threatening or involving the macula must be treated without delay. However, extramacular tractional detachments may be observed, since they often remain stationary for prolonged periods of time.

c. Combined tractional and rhegmatogenous RD should be treated urgently, even if the macula is not involved, because subretinal fluid is likely to spread quickly to involve the macula.

d. Premacular subhyaloid haemorrhage, if dense (Fig. 14.47) and persistent, should be considered for vitrectomy because, if untreated, the internal limiting membrane or posterior hyaloid face may serve as a scaffold for subsequent fibrovascular proliferation and

Fig. 14.47
Preretinal haemorrhage obscuring the posterior pole

subsequent tractional macular detachment or macular pucker caused by contraction of epiretinal membranes.

e. Macular oedema may occasionally benefit from pars plana vitrectomy as previously mentioned.

2. Aims

a. Removal of vitreous gel, thus eliminating the scaffold along which further fibrovascular tissue can proliferate. If this goal is achieved, involution of existing neovascular tissue also frequently occurs.

b. Removal of vitreous haemorrhage.

c. Repair of RD by excising tractional membranes (Fig. 14.48a) and removing fibrovascular tissue from the retinal surface. Any retinal breaks should also be sealed.

d. Prevention of further neovascularization by laser endophotocoagulation (Fig. 14.48b).

3. Complications

a. Progressive rubeosis iridis is the most common anterior segment complication resulting in failure. It has an increased incidence in aphakic eyes and in those with residual areas of detached retina. In eyes with total retinal detachments the incidence of rubeosis is virtually 100%.

b. Cataract may be the result of progression of pre-existing lens opacities or surgical trauma.

c. Glaucoma may be secondary to rubeosis or may be of the ghost cell or red cell type (*see* Chapter 9).

d. Recurrent vitreous haemorrhage may be caused by fresh fibrovascular proliferation.

e. Retinal detachment may be caused by operative complications, such as traction on the vitreous base or the inadvertent creation of fresh breaks with the cutter or other instruments. It may also occur later as a result of fresh fibrovascular proliferation.

4. Visual results depend on the specific indications for surgery and the complexity of pre-existing vitreoretinal abnormalities. In general, about 70% of cases achieve visual improvement, about 10% are made worse and the remainder have no change in vision. It appears that the first few postoperative months are vital. If an eye is doing well after 6 months, then the long-term outlook is favourable because the incidence of subsequent vision-threatening complications is low. Factors associated with a favourable prognosis are:

- Good preoperative visual function.
- Age of 40 years or less.
- Absence of preoperative rubeosis iridis and glaucoma.
- PRP of at least one-quarter of the fundus.

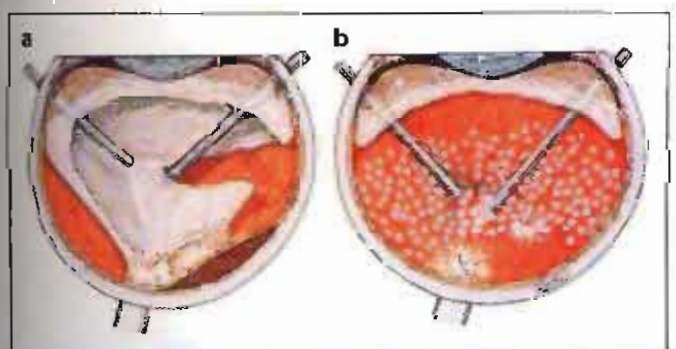


Fig. 14.48
Principles of vitreous surgery for advanced diabetic eye disease. (a) Retinal reattachment by excision of tractional forces; (b) endophotocoagulation

Screening for diabetic retinopathy

All diabetics aged over 12 years and/or entering puberty should be screened, and those with risk factors for visual loss referred to an ophthalmologist. Screening involves measurement of visual acuity for distance and near, and fundus examination following pupillary dilatation with tropicamide 1%.

1. Annual review but referral not appropriate
- Normal fundus.
- Mild BDR with small haemorrhages and/or small hard exudates more than one disc diameter from the fovea.

2. Routine referral to ophthalmologist
- BDR with large circinate exudates within the major temporal arcades but not threatening the fovea.
- BDR without maculopathy but with reduced visual acuity to determine the cause of visual impairment.

3. Early referral to ophthalmologist
- BDR with hard exudates and/or haemorrhages within one disc diameter from the fovea.
- Maculopathy.
- PPDR.

4. Urgent referral to ophthalmologist
- PDR.
- Preretinal or vitreous haemorrhage.
- Rubeosis iridis.
- Retinal detachment.

Retinal vein occlusion

Introduction

Classification

1. Branch retinal vein occlusion (BRVO).
2. Central retinal vein occlusion (CRVO).
- Non-ischaemic.
- Ischaemic.
- Papillophlebitis.

3. Hemiretinal vein occlusion.

Pathogenesis

Arteriolosclerosis is an important contributing factor for BRVO. Because a retinal arteriole and its corresponding vein share a common adventitial sheath, thickening of the arteriole appears to compress the vein if the arteriole is anterior to the vein. This causes secondary changes, including venous endothelial cell loss, thrombus formation

and eventually occlusion. Similarly, the central retinal vein and artery share a common adventitial sheath posterior to the lamina cribrosa so that atherosclerotic changes of the artery may compress the vein and precipitate CRVO. It therefore appears that both arterial and venous disease contribute to retinal vein occlusion. Venous occlusion causes elevation of venous and capillary pressure with stagnation of blood flow. Stagnation results in hypoxia of the retina drained by the obstructed vein, which in turn results in damage to the capillary endothelial cells and extravasation of blood constituents. The tissue pressure is increased, causing further stagnation of the circulation and hypoxia, so that a vicious cycle is established.

Underlying associations

In order of importance the following conditions are associated with an increased risk of retinal vein occlusion:

1. **Advancing age** is the most important factor; over 50% of cases occur in patients over the age of 65 years.
2. **Systemic** conditions include hypertension, hyperlipidaemia, diabetes, smoking and obesity.
3. **Raised intraocular pressure** (e.g. primary open-angle glaucoma, ocular hypertension) increases the risk of CRVO.
4. **Inflammatory** diseases such as sarcoidosis and Behçet disease may be associated with occlusive retinal periphlebitis.
5. **Hyperviscosity** associated with polycythaemia or abnormal plasma proteins (e.g. myeloma, Waldenström macroglobulinaemia).
6. **Acquired thrombophilic** disorders include hyperhomocysteinaemia and antiphospholipid antibody syndrome. Elevated plasma homocysteine is also a risk factor for myocardial infarction, stroke and carotid disease as well as CRVO, particularly the ischaemic type. Hyperhomocysteinaemia is readily reversible in most cases with folic acid.
7. **Inherited thrombophilic** disorders may be associated with venous occlusion in young adults. These include increased levels of clotting factors VII and XI, deficiencies of anticoagulants such as antithrombin III, protein C and S, and resistance to activated protein C (factor V Leiden).

NB: Factors that appear to decrease the risk of venous occlusion include increased physical activity and moderate alcohol consumption.

Branch retinal vein occlusion

Classification

1. **Major branch vein occlusion** may be subdivided as follows:
   - Occlusion of a first-order temporal branch at the optic disc (Fig. 14.49a and *see* Fig. 14.52a)).
   - Occlusion of a first-order temporal branch away from the disc but involving the branches to the macula (Figs 14.49b and 14.50).

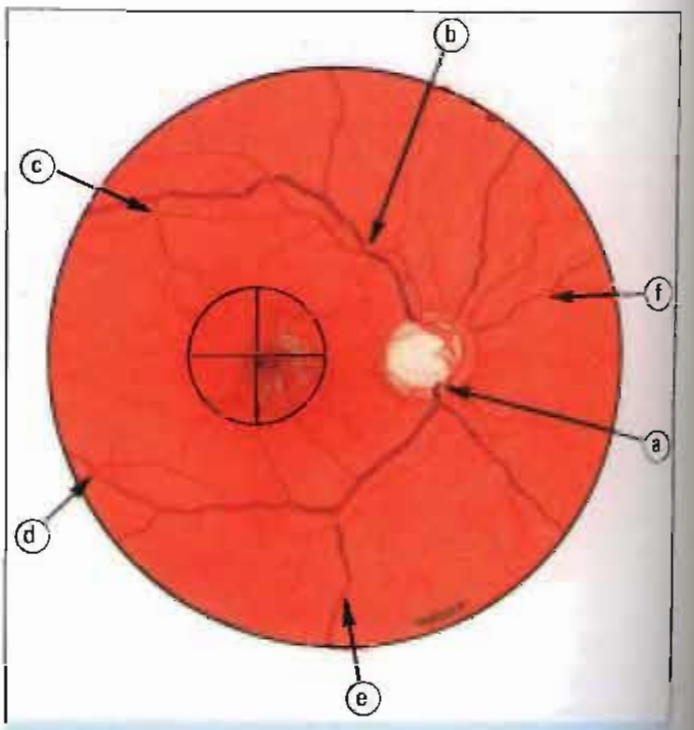


Fig. 14.49
Classification of retinal branch vein occlusion according to site of blockage (see *text*)

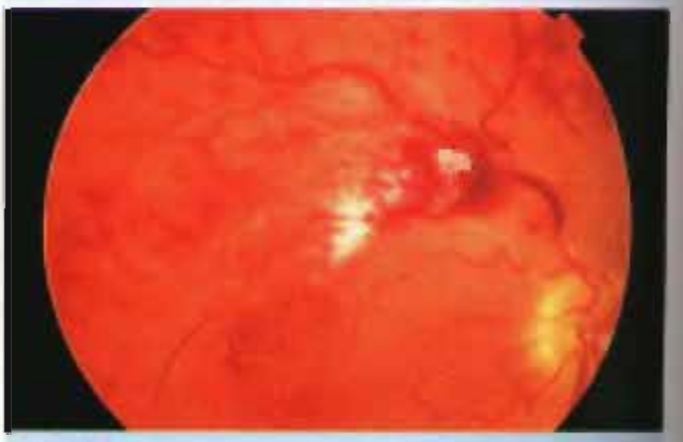


Fig. 14.50
Superotemporal branch retinal vein occlusion

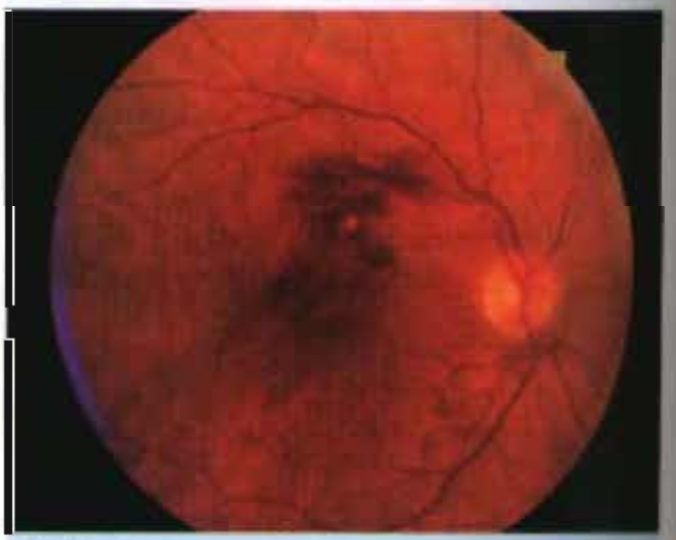


Fig. 14.51
Macular branch retinal vein occlusion

2. **Minor macular branch occlusion** involving only a macular branch (Figs 14.49c and 14.51).
3. **Peripheral branch occlusion** not involving the macular circulation (Fig. 14.49d–f).

Clinical features

1. **Presentation** depends on the amount of macular drainage compromised by the occlusion. Patients with macular involvement often present with sudden onset of blurred vision and metamorphopsia or a relative visual field defect. Patients with peripheral occlusions may be asymptomatic.
2. **Visual acuity** is variable and dependent on the extent of macular involvement.
3. **Fundus** (Fig. 14.52a)
   - Venous dilatation and tortuosity peripheral to the site of occlusion.
   - Flame-shaped and dot-blot haemorrhages, retinal oedema, and cotton wool spots affecting the sector of the retina drained by the obstructed vein.
4. **FA** during the early phases shows hypofluorescence due to blockage of background choroidal fluorescence by retinal haemorrhages (Fig. 14.52b and c). The late phase shows hyperfluorescence due to leakage (Fig. 14.52d).
5. **Course.** The acute features take 6–12 months to resolve and may be replaced by the following:
   - Venous sheathing and sclerosis peripheral to the site of obstruction with variable amount of residual haemorrhage (Fig. 14.53).
   - Collateral venous channels, characterized by slightly tortuous vessels, develop locally (Fig. 14.54), across the horizontal raphe between the inferior and superior vascular arcades, or at the optic disc (Fig. 14.55).
   - Microaneurysms and hard exudates (Fig. 14.56) may be associated with cholesterol crystal deposition.
   - The macula may show RPE changes or epiretinal gliosis.

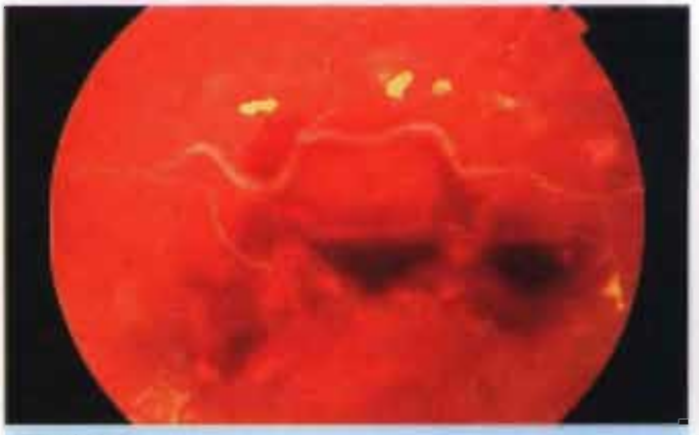


Fig. 14.53
Old superotemporal branch retinal vein occlusion showing venous sheathing, residual haemorrhages and a few hard exudates

Prognosis

This is reasonably good. Within 6 months about 50% of eyes develop efficient collaterals, with return of visual acuity to 6/12 or better. Eventual visual recovery depends on the amount of venous drainage involved by the occlusion (which is related to the site and size of the occluded vein) and the

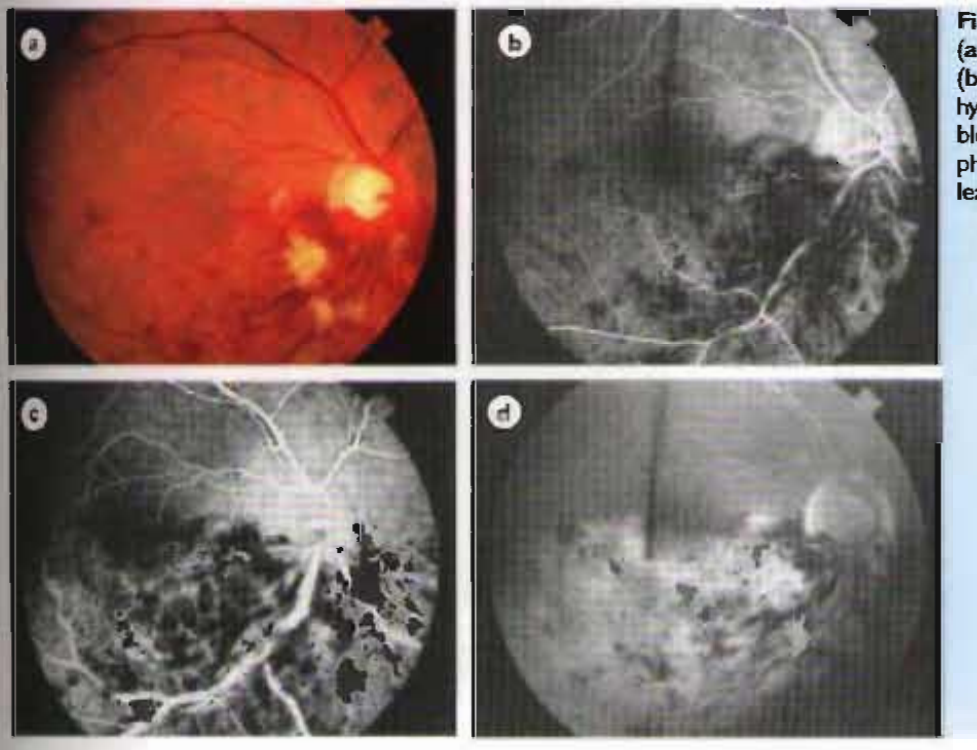


Fig. 14.52
(a) Major branch retinal vein occlusion; (b and c) venous phase FA showing hypofluorescence due to masking by blood and cotton wool spots; (d) late phase showing hyperfluorescence due to leakage (Courtesy of S. Milewski)

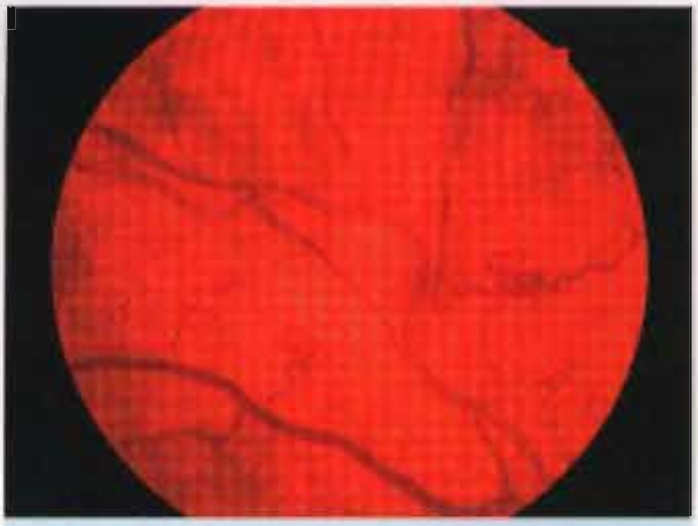


Fig. 14.54
Collaterals following branch retinal vein occlusion

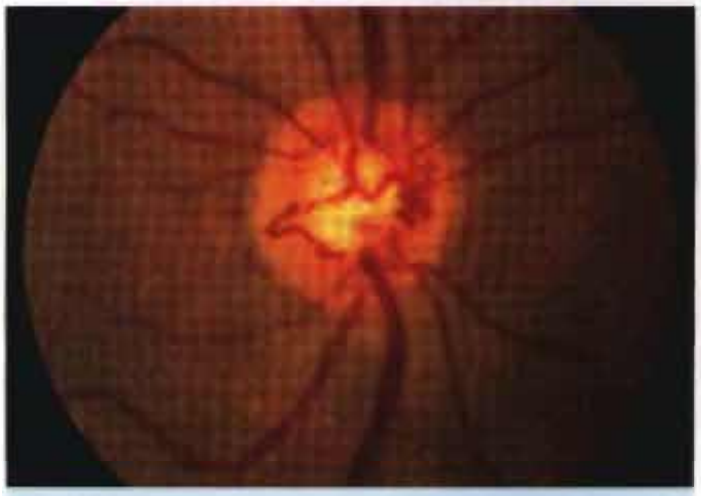


Fig. 14.55
Disc collaterals following non-ischaemic central retinal vein occlusion

severity of macular ischaemia. The two main vision-threatening complications are:

1. **Chronic macular oedema** is the most common cause of persistent poor visual acuity after BRVO. Some patients with visual acuity of 6/12 or worse may benefit from laser photocoagulation, provided the macula is oedematous rather than ischaemic.
2. **Neovascularization**. NVD develops in about 10% and NVE in 20–30% of eyes. The incidence of both increases with the severity and extent of involvement. NVE usually develops at the border of the triangular sector of ischaemic retina non-drained by the occluded vein. Neovascularization may develop at any time within the first 3 years but usually appears during the initial 6–12 months. It is a serious complication because it can lead to recurrent vitreous and preretinal haemorrhage, and occasionally tractional retinal detachment.

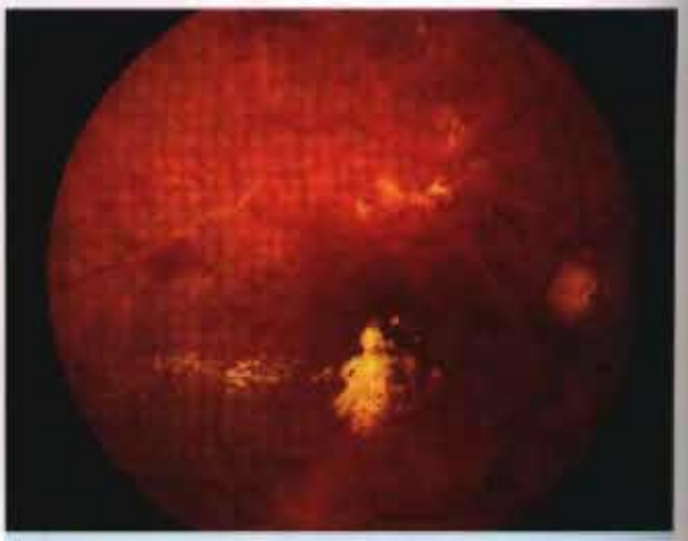


Fig. 14.56
Hard exudates at the macula following a superotemporal branch retinal vein occlusion

Follow-up

The patient should be reviewed at 6–12 weeks with FA, provided the retinal haemorrhages have cleared sufficiently. Further management depends on visual acuity and angiographic findings.

- FA shows good macular perfusion and visual acuity is improving—no treatment is required.
- FA shows macular oedema associated with good macular perfusion (Fig. 14.57) and visual acuity continues to be 6/12 or worse after 3 months—laser photocoagulation should be considered. However, prior to treatment, the FA should be studied carefully to identify the leaking areas. It

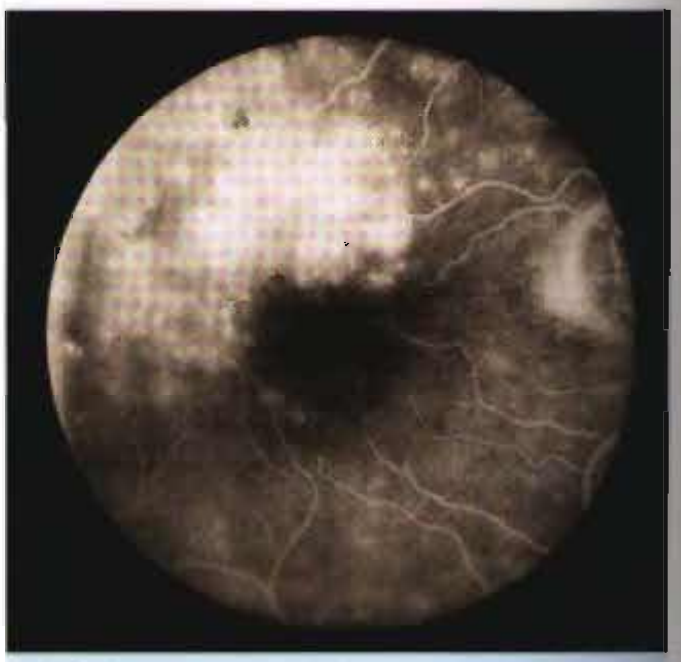


Fig. 14.57
FA showing extensive leakage but good macular perfusion following a superotemporal branch vein occlusion

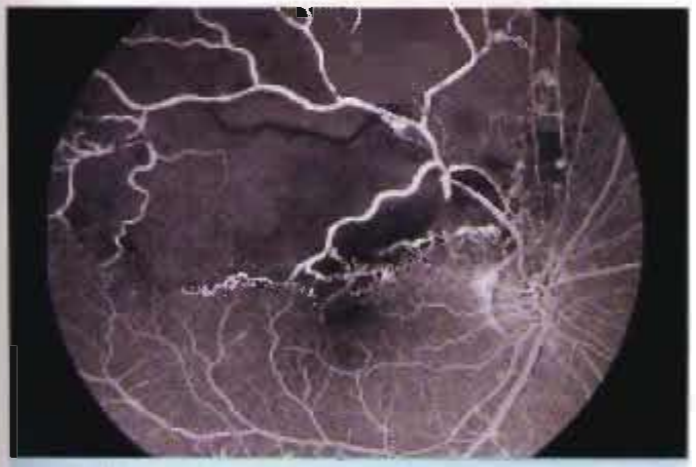


Fig. 14.58
FA showing extensive capillary closure following a superotemporal branch retinal vein occlusion

is also very important to identify collateral vessels, which do not leak fluorescein, because they must not be treated.

- FA shows macular non-perfusion (Fig. 14.58) and visual acuity is poor—laser treatment will not improve vision. However, if the FA shows five or more disc diameters of non-perfusion the patient should be reviewed at 4-monthly intervals for 12–24 months because of the risk of neovascularization.

Laser treatment

1. **Macular oedema** is treated by grid laser photocoagulation (50–100 μm burns spaced one burn apart) to produce a medium reaction to the area of leakage as identified on FA. The burns should extend no closer to the fovea than the edge of the FAZ and be no more peripheral than the major vascular arcades. Care should be taken to avoid treating over intraretinal haemorrhage. Follow-up should be after 2–3 months. If macular oedema persists re-treatment may be considered although the results may be disappointing.
2. **Neovascularization** is treated by scatter laser photocoagulation (200–500 μm burns one burn apart) to achieve a medium reaction covering the entire involved sector as defined by the colour photograph and FA. Follow-up should be after 4–6 weeks. If neovascularization persists re-treatment is frequently effective in inducing regression.

Non-ischaemic central retinal vein occlusion

Non-ischaemic CRVO is the most common type, accounting for about 75% of all cases.

Clinical features

1. **Presentation** is with sudden, unilateral blurred vision.
2. **Visual impairment** is moderate to severe.
3. **APD** (afferent pupillary defect) is absent or mild (in contrast to ischaemic CRVO).
4. **Fundus** (Fig. 14.59a)
   - Variable tortuosity and dilatation of all branches of the central retinal vein.
   - Retinal dot-blot and flame-shaped haemorrhages, throughout all four quadrants and most numerous in the periphery.
   - Occasional cotton wool spots.

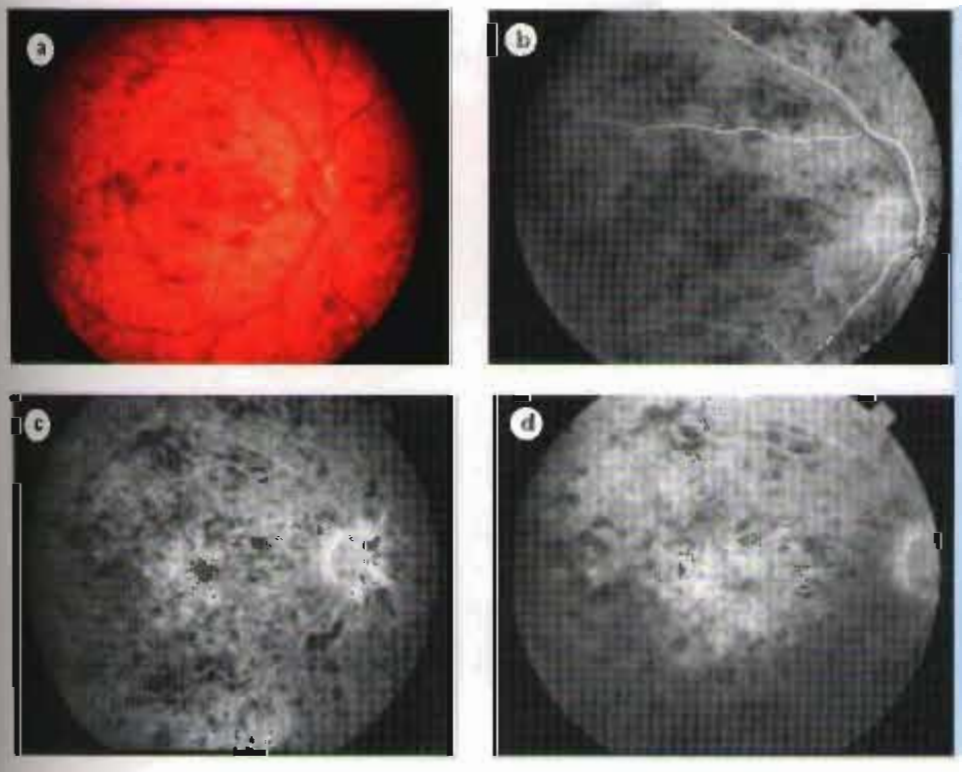


Fig. 14.59
(a) Non-ischaemic central retinal vein occlusion; **(b)** arteriovenous phase showing blockage of fluorescence by haemorrhages; **(c)** late venous phase showing early hyperfluorescence at the macula due to leakage; **(d)** late phase showing marked hyperfluorescence due to progressive leakage (Courtesy of S. Milewski)

- Mild to moderate optic disc oedema and macular oedema are common.

5. **FA** shows delayed venous return, good retinal capillary perfusion (Fig. 14.59b and c) and late leakage (Fig. 14.59d).
6. **Course.** Most acute signs resolve over 6–12 months. Residual findings include disc collaterals, epiretinal gliosis and pigmentary changes at the macula. Conversion to ischaemic CRVO occurs in 15% of cases within 4 months and 34% within 3 years.

Prognosis

In cases that do not subsequently become ischaemic, prognosis is reasonably good, with return of visual acuity to normal or near normal in about 50%. The main cause for poor visual acuity is chronic CMO which may lead to secondary RPE changes. To a certain extent prognosis depends on initial visual acuity as follows:

- If initial visual acuity is 6/18 or better, it is likely to remain so.
- If visual acuity is 6/24–6/60, the clinical course is variable, and vision may subsequently improve, remain the same, or worsen.
- If visual acuity at the onset is worse than 6/60, improvement is unlikely.

Management

1. **Follow-up** should be for 3 years to detect conversion to ischaemic CRVO.
2. **Treatment** by high-intensity laser to create an anastomosis between a retinal vein and a choroidal vein, thereby bypassing the site of obstruction to venous outflow, may be beneficial in some cases but is not without potential risks such as fibrous proliferation at the laser site (Fig. 14.60), and haemorrhage from the ruptured vein or from vessels in the choroid. Chronic CMO is unresponsive to laser therapy.

Ischaemic central retinal vein occlusion

Clinical features

1. **Presentation** is with unilateral, sudden and severe visual impairment.
2. **Visual impairment** is profound.
3. **APD** is marked.
4. **Fundus** (Fig. 14.61a)
   - Marked tortuosity and engorgement of all branches of the central retinal vein.
   - Extensive dot-blot and flame-shaped haemorrhages involving the peripheral retina and posterior pole.

Fig. 14.60
Fibrous proliferation at site of laser-induced anastomosis for non-ischaemic central retinal vein occlusion.

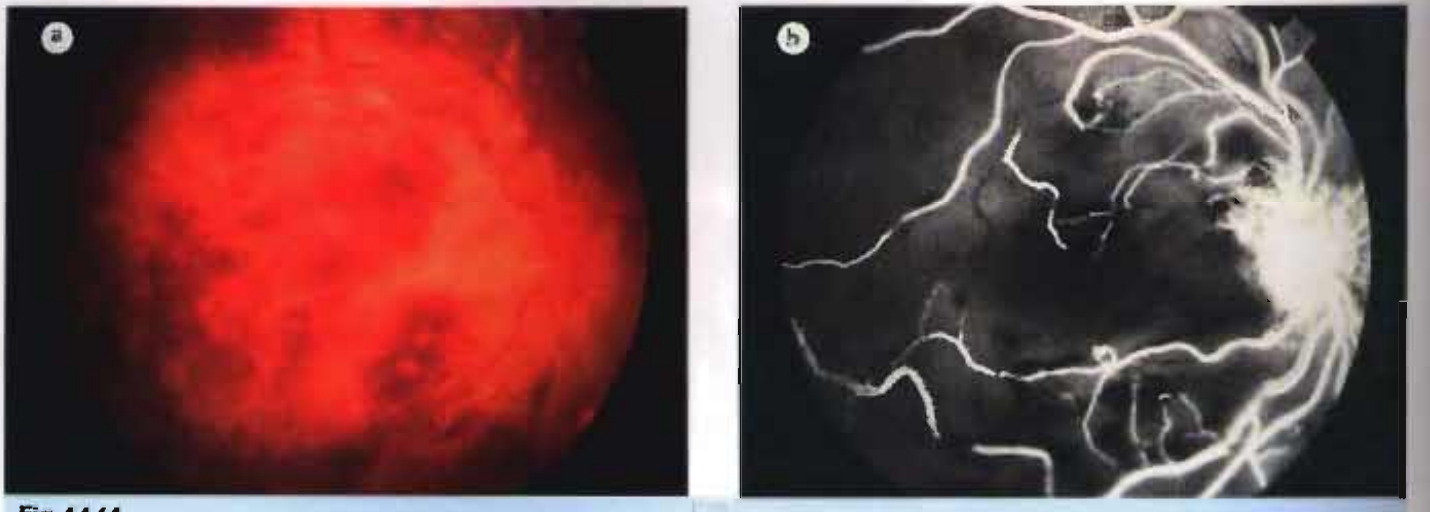


Fig. 14.61
(a) Ischaemic central retinal vein occlusion; (b) FA showing extensive capillary non-perfusion

- Cotton wool spots, which may be numerous.
- Macular oedema and haemorrhage.
- Severe optic disc oedema and hyperaemia.

5. **FA** shows central masking by retinal haemorrhages and extensive areas of capillary non-perfusion (Fig. 14.61b).
6. **Course.** Most acute signs resolve over the next 9–12 months. Residual findings include disc collaterals, macular epiretinal gliosis and pigmentary changes. Rarely subretinal fibrosis resembling that associated with exudative age-related macular degeneration may develop.
7. **Prognosis** is extremely poor due to macular ischaemia. Rubeosis iridis develops in about 50% of eyes, usually between 2 and 4 months (100-day glaucoma), and unless treated vigorously with PRP there is a high risk of neovascular glaucoma (*see* Chapter 9).

Management

1. **Follow-up** should be monthly for 6 months in order to detect anterior segment neovascularization. Angle neovascularization, while not synonymous with eventual neovascular glaucoma, is the best clinical predictor of the eventual risk of neovascular glaucoma because it may occur in the absence of neovascularization at the pupillary margin.

> *NB:* Routine gonioscopy of eyes at risk should therefore be performed; mere slit-lamp examination of the iris is inadequate.

2. **Treatment.** PRP (Fig. 14.62) should be performed without delay in eyes with angle or iris neovascularization. Prophylactic laser therapy is appropriate only if regular follow-up is not possible. Unfortunately, retinal haemorrhages often have not cleared sufficiently by the time photocoagulation becomes necessary.

Fig. 14.62
Appearance following laser panretinal photocoagulation for early rubeosis associated with ischaemic central retinal vein occlusion

Fig. 14.63
Papillophlebitis

Papillophlebitis

Papillophlebitis (optic disc vasculitis), is an uncommon condition which typically affects otherwise healthy individuals under the age of 50 years. It is thought that the underlying lesion is optic disc swelling with resultant secondary venous congestion rather than venous thrombosis occurring at the level of the lamina cribrosa as occurs in older patients.

1. **Presentation** is with relatively mild blurring of vision typically worst on waking.
2. **Visual impairment** is mild to moderate.
3. **APD** is absent.
4. **Fundus** (Fig. 14.63)
   - Disc oedema, which may be associated with cotton wool spots, is the dominant finding.
   - Venous dilatation and tortuosity with variable amount of retinal haemorrhages, usually confined to the parapapillary area and posterior fundus.
5. **Blind spot** is enlarged.
6. **FA** shows delay in venous filling, hyperfluorescence due to leakage and good capillary perfusion.
7. **Prognosis** is excellent despite the lack of treatment. Eighty per cent of cases achieve a final visual acuity of 6/12 or better. The remainder suffer significant and permanent visual impairment as a result of macular oedema.

Hemiretinal vein occlusion

Hemiretinal vein occlusion is less common than both BRVO and CRVO. It involves occlusion of the superior or inferior branch of the CRV.

1. **Classification**
   a. ***Hemisphere*** occlusion of a major branch of the CRV at or near the optic disc.
   b. ***Hemicentral*** occlusion, which is less common, involves one trunk of a dual-trunked CRV, which persists in the anterior part of the optic nerve head as a congenital variant.

Fig. 14.64
Inferior hemiretinal vein occlusion

2. **Presentation** is with a sudden altitudinal visual field defect.
3. **Visual impairment** is variable.
4. **Fundus.** This shows the features of BRVO, involving the superior or inferior hemisphere (Fig. 14.64).
5. **FA** shows masking by haemorrhages, hyperfluorescence due to leakage and variable retinal capillary non-perfusion.
6. **Prognosis** is dependent on the severity of macular ischaemia and oedema.
7. **Treatment** depends on the severity of retinal ischaemia. Extensive retinal ischaemia carries the risk of neovascular glaucoma and should be managed in the same way as ischaemic CRVO.

Retinal artery occlusion

Introduction

Classification

1. **Branch retinal artery occlusion (BRAO).**
2. **Central retinal artery occlusion (CRAO).**
3. **Cilioretinal artery occlusion.**

Causes

1. **Atherosclerosis-related thrombosis** at the level of the lamina cribrosa is by far the most common underlying cause of CRAO, accounting for about 80% of cases.
2. **Carotid embolism** originating from the bifurcation of the common carotid artery. This is a vulnerable site for

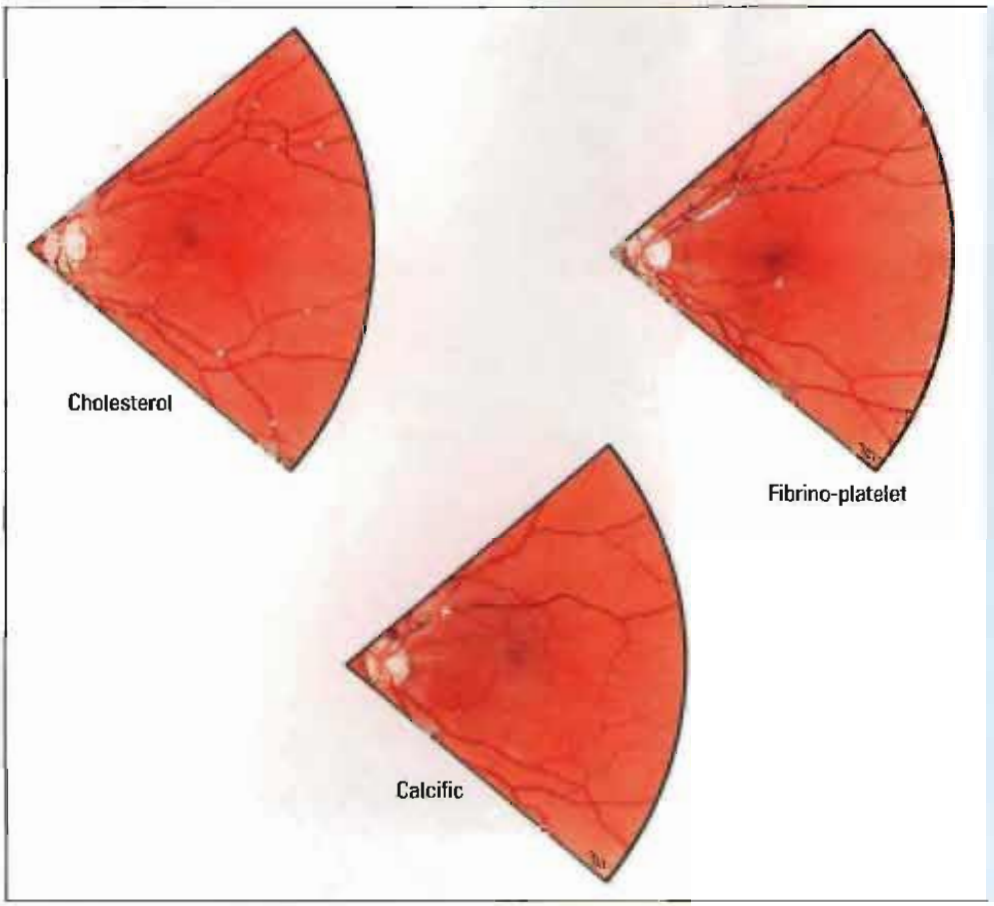


Fig. 14.65
Main types of retinal emboli

Fig. 14.66
Cholesterol emboli (Hollenhorst plaques)

atheromatous ulceration and stenosis (*see* Chapter 20). Retinal emboli from the carotid arteries may be of the following types (Fig. 14.65):

a. ***Cholesterol*** emboli (Hollenhorst plaques) appear as intermittent showers of minute, bright, refractile, golden to yellow-orange crystals, often located at arteriolar bifurcations (Fig. 14.66). They rarely cause significant obstruction to the retinal arterioles and are frequently asymptomatic.

b. ***Fibrinoplatelet*** emboli are dull grey, elongated particles which are usually multiple and occasionally fill the entire lumen (Fig. 14.67). They may cause a retinal transient ischaemic attack (TIA), with resultant amaurosis fugax, and occasionally complete obstruction. Amaurosis fugax is characterized by painless transient unilateral loss of vision, often described as a curtain coming down over the eye, usually from top to bottom, but occasionally vice versa. Visual loss, which may be complete, usually lasts a few minutes. Recovery is in the same pattern as the initial loss, although usually more gradual. Frequency of attacks may vary from several times a day to once every few months. The attacks may be associated with ipsilateral cerebral TIA with contralateral signs.

c. ***Calcific*** emboli may originate from atheromatous plaques in the ascending aorta or carotid arteries, as well as from calcified heart valves. They are usually single, white, non-scintillating and often close to the disc (Fig. 14.68). When located on the disc itself, they may easily be overlooked because they tend to merge with the disc. Calcific emboli are much more dangerous than the other two kinds because they may cause permanent occlusion of the central retinal artery or one of its main branches.

3. **Giant cell arteritis.**
4. **Cardiac embolism** is responsible for about 20% of retinal arterial occlusions and is associated with an increased risk of cerebrovascular disease. Since the ophthalmic artery is the first branch of the internal carotid artery, embolic material from the heart and carotid arteries has a fairly direct route to the eye. Emboli originating from the heart and its valves may be of the following four types:
   a. ***Calcific*** from the aortic or mitral valves.
   b. ***Vegetations*** from cardiac valves in bacterial endocarditis.
   c. ***Thrombus*** from the left side of the heart, consequent to myocardial infarction (mural thrombi), mitral stenosis associated with atrial fibrillation or mitral valve prolapse.
   d. ***Myxomatous material*** from the very rare atrial myxoma.
5. **Periarteritis** associated with dermatomyositis, systemic lupus erythematosus, polyarteritis nodosa, Wegener granulomatosis and Behçet disease may occasionally be responsible for BRAO, which may be multiple (Fig. 14.69).

Fig. 14.67
Fibrinoplatelet emboli

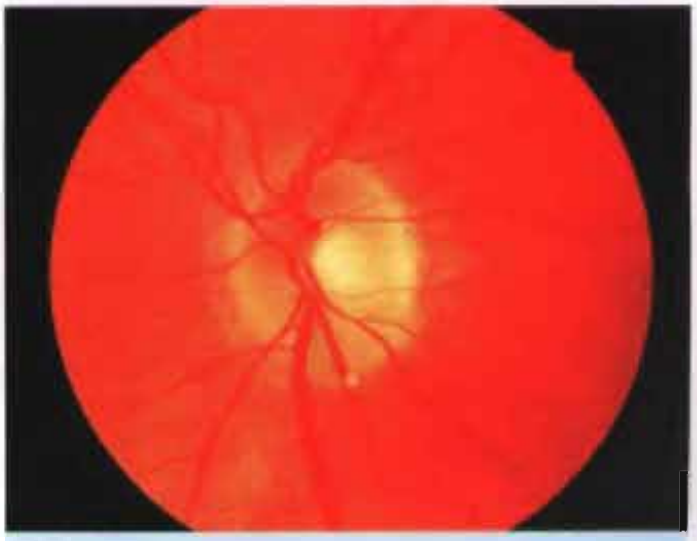


Fig. 14.68
Calcific embolus at the inferior edge of the disc

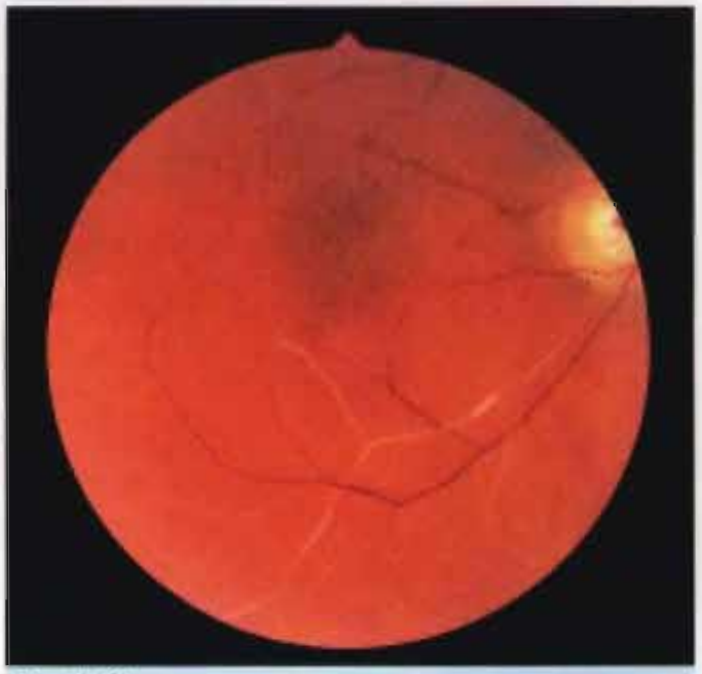


Fig. 14.69
Multiple branch retinal artery occlusions in polyarteritis nodosa

6. **Thrombophilic disorders** such as hyperhomocysteinaemia, antiphospholipid antibody syndrome and inherited defects of natural anticoagulants may occasionally be associated with retinal artery obstruction in young individuals.
7. **Retinal migraine** may very rarely be responsible for retinal artery occlusion in young individuals. However, the diagnosis should be made only after other more common causes have been excluded.

Branch retinal artery occlusion

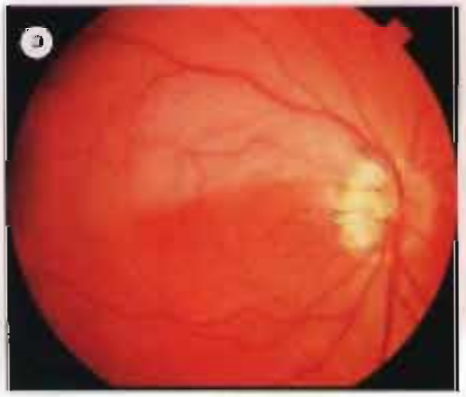
BRAO is most frequently caused by embolism and occasionally by periarteritis.

1. **Presentation** is with sudden and profound altitudinal or sectoral visual field loss.
2. **Visual impairment** is variable.
3. **Fundus** (Fig. 14.70a)
   - Retinal cloudiness corresponding to the area of ischaemia resulting from oedema.
   - Narrowing of arteries and veins with sludging and segmentation of the blood column.
   - One or more emboli may be present.
4. **FA** shows delay in arterial filling and masking of background fluorescence by retinal swelling which is confined to the involved sector (Fig. 14.70b).
5. **Prognosis** is poor unless the obstruction can be relieved within a few hours (*see* below). The visual field defect is permanent and the affected artery remains attenuated. Occasionally, however, recanalization of the obstructed artery may leave subtle or absent ophthalmoscopic signs.

Central retinal artery occlusion

CRAO is most frequently the result of atherosclerosis, although it may also be caused by calcific emboli.

1. **Presentation** is with sudden and profound loss of vision.
2. **Visual impairment** is profound except when a portion of the papillomacular bundle is supplied by a cilioretinal artery, when central vision may be preserved.
3. **APD** is profound or total (amaurotic pupil).
4. **Fundus**
   - Attenuation of arteries and veins with sludging and segmentation of the blood column (cattle-trucking) (Fig. 14.71).
   - Extensive retinal cloudiness (Fig. 14.72).
   - The orange reflex from the intact choroid stands out at the thin foveola, in contrast to the surrounding pale retina, giving rise to the 'cherry-red spot' appearance (Fig. 14.73).
   - In eyes with a cilioretinal artery part of the macula will remain of normal colour (Fig. 14.74a).
5. **FA** shows delay in arterial filling and masking of background choroidal fluorescence by retinal swelling. However, a patent cilioretinal artery will fill during the early phase (Fig. 14.74b).
6. **Prognosis** is poor due to retinal infarction. After a few weeks the retinal cloudiness and the 'cherry-red spot' disappear although the arteries remain attenuated



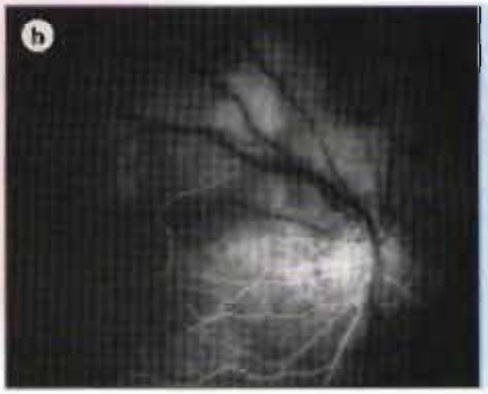


Fig. 14.70
(a) Superotemporal branch retinal artery occlusion; (b) FA showing hypofluorescence of the involved sector due to absence of arterial filling and blockage of background fluorescence by oedema (Courtesy of S. Milewski)

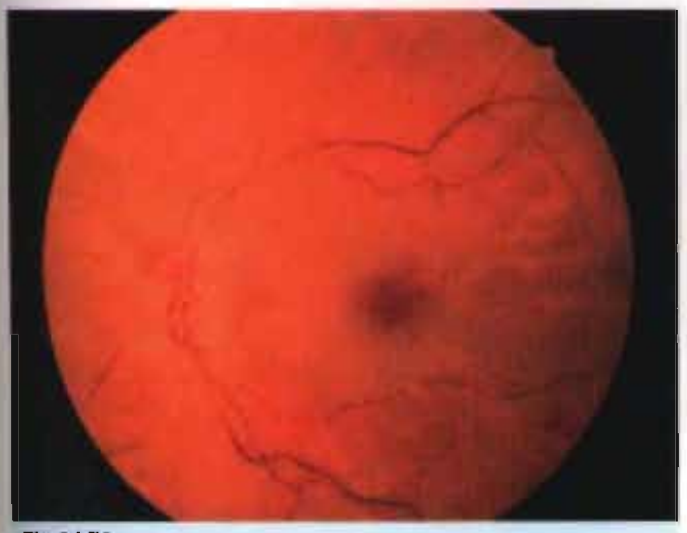


Fig. 14.71
Acute central retinal artery occlusion showing vascular attenuation and segmentation of the blood column (cattle-trucking)

Fig. 14.72
Severe retinal clouding in acute central retinal artery occlusion with sparing of the territory supplied by a cilioretinal artery

(Fig. 14.75). The inner retinal layers become atrophic and consecutive optic atrophy ensures permanent loss of all useful vision. Some eyes develop rubeosis iridis which may require PRP, and about 2% develop NVD.

Cilioretinal artery occlusion

A cilioretinal artery, present in 20% of the population, arises from the posterior ciliary circulation but supplies the retina, commonly in the area of the macula and papillomacular bundle.

I. Classification

a. isolated (Fig. 14.76) typically affects young patients with an associated systemic vasculitis.

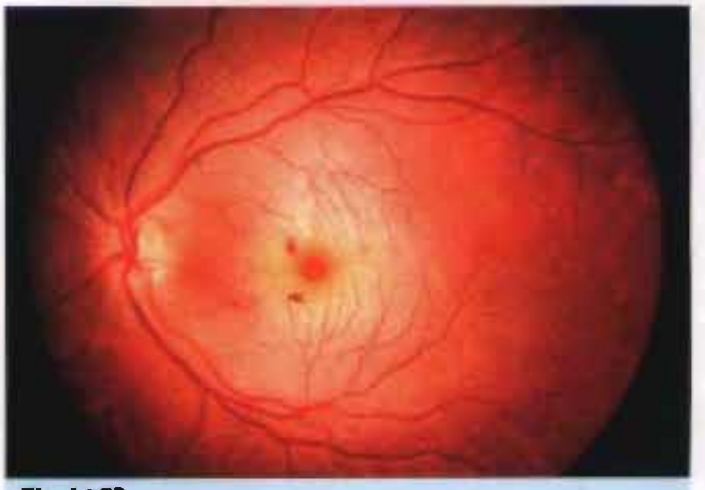


Fig. 14.73
Cherry-red spot at the foveola in acute central retinal artery occlusion (Courtesy of C. Barry)

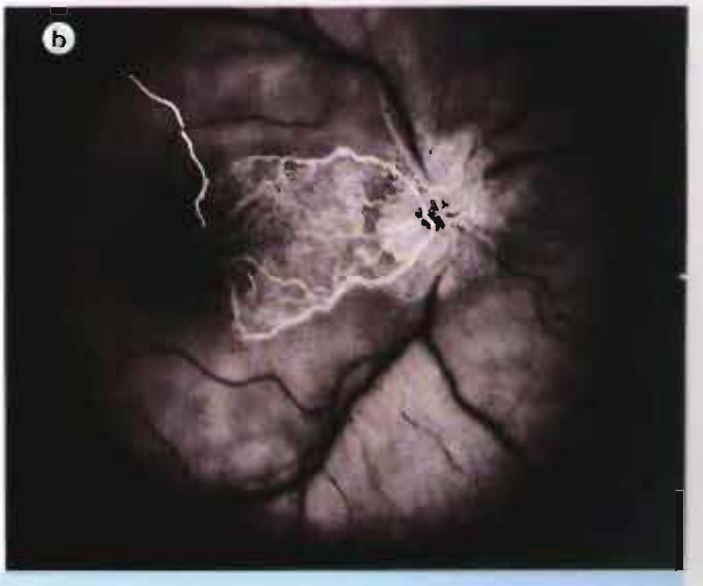


Fig. 14.74
(a) Acute central retinal artery occlusion with sparing of a cilioretinal artery; (b) FA showing perfusion only of the macula

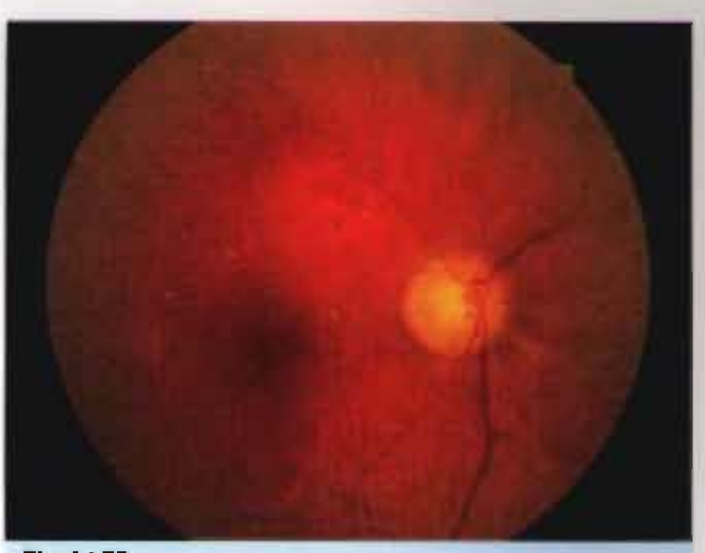


Fig. 14.75
Vascular attenuation and consecutive optic atrophy following central retinal artery occlusion

Fig. 14.76
Isolated cilioretinal artery occlusion (Courtesy of S. Milewski)

Fig. 14.77
Combined cilioretinal artery and central retinal vein occlusion

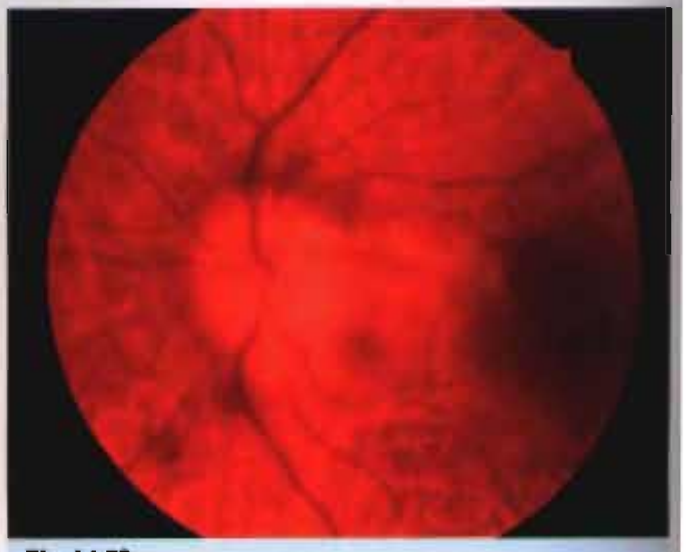


Fig. 14.78
Combined cilioretinal artery occlusion and anterior ischaemic optic neuropathy

Fig. 14.79
FA of isolated cilioretinal artery occlusion showing hypofluorescence at the macula due to lack of filling and blockage of background choroidal fluorescence (Courtesy of S. Milewski)

   b. ***Combined with CRVO*** (Fig. 14.77) has a similar prognosis to non-ischaemic CRVO.
   c. ***Combined with anterior ischaemic optic neuropathy*** (Fig. 14.78) typically affects patients with giant cell arteritis and carries a very poor prognosis.
2. **Presentation** is with acute, severe loss of central vision.
3. **Fundus**. Cloudiness localized to that part of the retina normally perfused by the vessel.
4. **FA** shows a corresponding filling defect (Fig. 14.79).

Treatment of acute retinal artery occlusion

Retinal artery occlusion is an emergency because it causes irreversible visual loss unless the retinal circulation is re-established prior to the development of retinal infarction. It appears that the prognosis for occlusions caused by calcific

emboli is worse than that resulting from either cholesterol or platelet emboli. Theoretically, timely dislodgement of emboli of the latter two types may prevent subsequent visual loss. To this end many mechanical and pharmacological methods have been tried. The following aggressive systematic stepwise approach gives the greatest chance of success in patients with occlusions of less than 48 hours duration at presentation.

Initial treatment

1. **Ocular massage** using a three-mirror contact lens for approximately 10 seconds, to obtain central retinal artery pulsation or cessation of flow (for BRAO), followed by 5 seconds of release. The aim is to mechanically collapse the arterial lumen and cause prompt changes in arterial flow.
2. **Sublingual isosorbide dinitrate** 10 mg to dilate peripheral blood vessels and decrease resistance.
3. **Lowering of intraocular pressure** with a combination of intravenous acetazolamide 500 mg, followed by intravenous mannitol 20% (1 g/kg) or oral glycerol 50% (1 g/kg).

Subsequent treatment

If the aforementioned measures are unsuccessful in re-establishing circulation after 20 minutes, subsequent treatment is as follows:

1. **Anterior chamber paracentesis.**
2. **Intravenous streptokinase** 750,000 units to disintegrate fibrin emboli, combined with intravenous methylprednisolone 500 mg to decrease the risk of streptokinase-related allergy and bleeding.
3. **Retrobulbar injection** of tolazoline 50 mg to decrease retrobulbar resistance to flow.

Ocular ischaemic syndrome

Pathogenesis

Ocular ischaemic syndrome is an uncommon condition which is the result of chronic ocular hypoperfusion secondary to severe ipsilateral atherosclerotic carotid stenosis. It typically affects patients during the seventh decade and may be associated with diabetes, hypertension, ischaemic heart disease and cerebrovascular disease. The 5-year mortality is of the order of 40%, most frequently from cardiac disease. Patients with ocular ischaemic syndrome may also give a history of amaurosis fugax due to retinal embolism.

Clinical features

The ocular ischaemic syndrome is unilateral in 80% of cases and affects both anterior and posterior segments. The signs are variable and may be subtle, so that the condition may be either missed or misdiagnosed.

1. **Presentation** is usually with gradual loss of vision over several weeks or months although occasionally visual loss may be sudden.
2. **Anterior segment**
   - Diffuse episcleral injection.
   - Corneal oedema and striae.
   - Aqueous flare with few if any cells (ischaemic pseudoiritis).
   - Mid-dilated and poorly reacting pupil.
   - Iris atrophy.
   - Rubeosis iridis is common and often progresses to neovascular glaucoma.
   - Cataract in very advanced cases.
3. **Fundus.** (Fig. 14.80)
   - Venous dilatation, with or without mild tortuosity, and arteriolar narrowing.
   - Microaneurysms, dot and blot haemorrhages and occasionally cotton wool spots.
   - Proliferative retinopathy with NVD and occasionally NVE.
   - Macular oedema.
   - Spontaneous arterial pulsation most pronounced near the optic disc is present in most cases or may be easily induced by exerting gentle pressure on the globe (digital ophthalmodynamometry).
4. **FA** shows delayed and patchy choroidal filling, prolonged arteriovenous transit time, retinal capillary non-perfusion, late leakage and prominent arterial staining.

Management

1. **Anterior segment manifestations** are treated with topical steroids and mydriatics.
2. **Neovascular glaucoma** may be treated medically or surgically (*see* Chapter 9).

Fig. 14.80
Arteriolar attenuation, venous dilatation, haemorrhages and NVD in ocular ischaemic syndrome

3. **Proliferative retinopathy** requires PRP although the results are less favourable than in proliferative diabetic retinopathy.

Differential diagnosis

1. **Non-ischaemic CRVO**
   - Similarities: unilateral retinal haemorrhages, venous dilatation and cotton wool spots.
   - Differences: normal retinal artery perfusion, haemorrhages are more numerous and mainly flame-shaped, disc oedema is present.
2. **Diabetic retinopathy**
   - Similarities: dot and blot retinal haemorrhages, venous tortuosity and proliferative retinopathy.
   - Differences: usually bilateral and hard exudates are present.
3. **Hypertensive retinopathy**
   - Similarities: arteriolar attenuation and focal constriction, haemorrhages and cotton wool spots.
   - Differences: invariably bilateral and absence of venous changes.

Hypertensive retinopathy

Systemic hypertension is diagnosed on blood pressure readings on several consecutive occasions of 140/90 or over (*see* Chapter 20).

Retinal changes

The primary response of the retinal arterioles to systemic hypertension is narrowing (vasoconstriction). However, the degree of narrowing is dependent on the amount of pre-existing replacement fibrosis (involutional sclerosis). For this reason, hypertensive narrowing is seen in its pure form only in young individuals. In older patients, rigidity of retinal arterioles due to involutional sclerosis prevents the same degree of narrowing seen in young individuals. In sustained hypertension the inner blood–retinal barrier is disrupted in small areas, with increased vascular permeability. The fundus picture of hypertensive retinopathy is therefore characterized by the following:

1. **Arterial narrowing** may be focal (Fig. 14.81) or generalized (Fig. 14.82). Ophthalmoscopic diagnosis of generalized narrowing is difficult, although the presence of focal narrowing makes it highly probable that blood pressure is raised. Severe hypertension may lead to obstruction of the precapillary arterioles and the development of cotton wool spots (Fig. 14.83).
2. **Vascular leakage** leads to flame-shaped retinal haemorrhages and retinal oedema (Fig. 14.84). Chronic retinal oedema may result in the deposition of hard exudates around the fovea in Henle layer with a macular star configuration (Fig. 14.85). Swelling of the optic nerve head is the hallmark of malignant hypertension (Fig. 14.86).

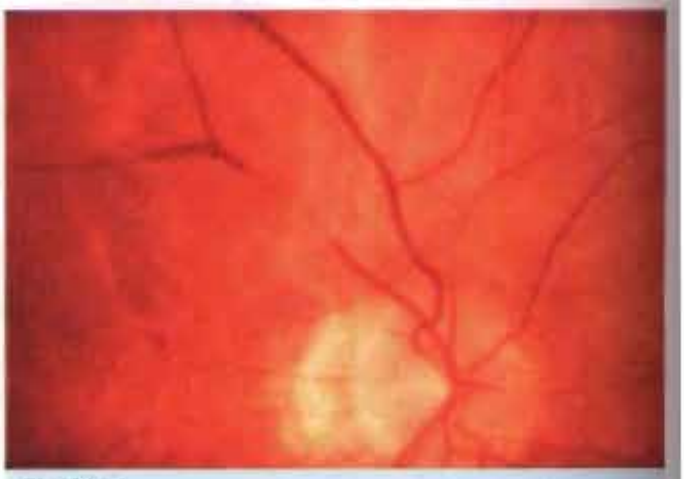


Fig. 14.81
Focal arterial narrowing in hypertension

Fig. 14.82
Generalized arterial narrowing in hypertension

Fig. 14.83
Arterial narrowing and a cotton wool spot in hypertension

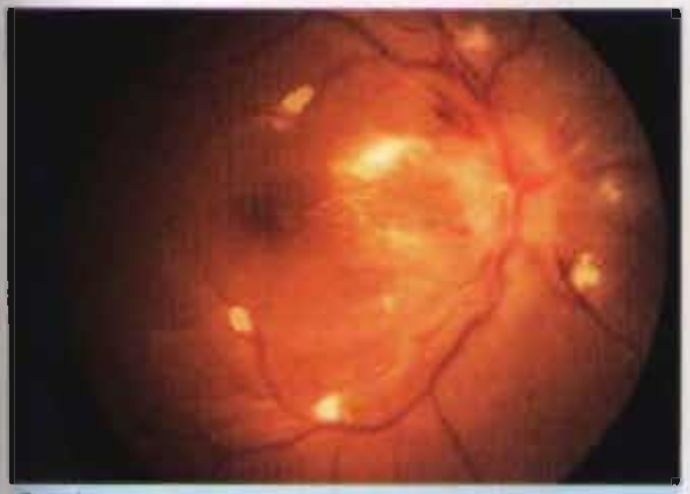


Fig. 14.84
Severe hypertensive retinopathy with cotton wool spots, flame-shaped haemorrhages, early macular star formation and mild disc swelling

Fig. 14.86
Very severe hypertensive retinopathy with severe disc oedema and a macular star

Fig. 14.85
Severe hypertensive retinopathy with a fully developed macular star, cotton wool spots, a few flame-shaped haemorrhages and moderate disc swelling

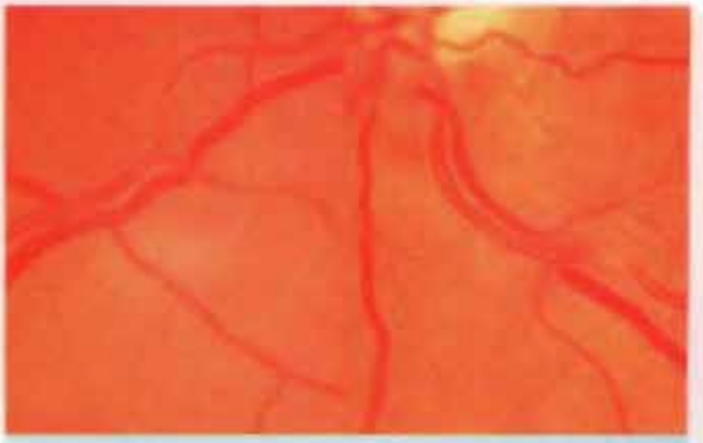


Fig. 14.87
Hypertensive changes at arteriovenous crossings

3. **Arteriolosclerosis** involves thickening of the vessel wall characterized histologically by intimal hyalinization, medial hypertrophy and endothelial hyperplasia. The most important clinical sign is the presence of changes at arteriovenous crossings (AV nipping) (Fig. 14.87), which although not necessarily indicative of the severity of hypertension, makes it probable that it has been present for many years. Mild changes at arteriovenous crossings are seen in patients with involutional sclerosis in the absence of hypertension. The grading of arteriolosclerosis is shown in Fig. 14.90.

Choroidal changes

These are rare but may occur as the result of an acute hypertensive crisis (accelerated hypertension) in young adults.

1. **Elschnig spots** are small, black spots surrounded by yellow haloes (Fig. 14.88) which represent focal choroidal infarcts.
2. **Siegrist streaks** are flecks arranged linearly along choroidal vessels (Fig. 14.89) which are indicative of fibrinoid necrosis associated with malignant hypertension.
3. **Exudative retinal detachment**, sometimes bilateral, may occur in severe acute hypertension such as that associated with toxaemia of pregnancy.

Fig. 14.88
Elschnig spots in hypertension

Fig. 14.89
Siegrist lines in hypertenion

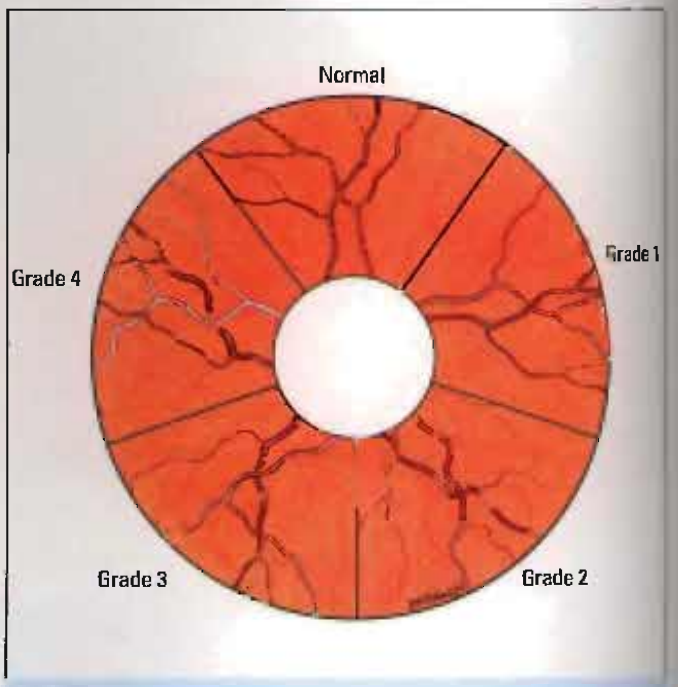


Fig. 14.90
Grading of retinal arteriolosclerosis (see *text*)

Grading of arteriolosclerosis (Fig. 14.90)

1. **Grade 1**. Subtle broadening of the arteriolar light reflex, mild generalized arteriolar attenuation, particularly of small branches, and vein concealment.
2. **Grade 2**. Obvious broadening of the arteriolar light reflex and deflection of veins at arteriovenous crossings (Salus sign).
3. **Grade 3**. Copper-wiring of arterioles, banking of veins distal to arteriovenous crossings (Bonnet sign), tapering of veins on either side of the crossings (Gunn sign) and right-angled deflection of veins.
4. **Grade 4**. Silver-wiring of arterioles and grade 3 changes.

Ocular associations and complications of hypertension

- Retinal vein occlusion.
- Retinal artery occlusion.
- Retinal artery macroaneurysm.
- Anterior ischaemic optic neuropathy.
- Ocular motor nerve palsy.
- Uncontrolled hypertension may adversely affect diabetic retinopathy.

Sickle-cell retinopathy

Introduction

Sickling haemoglobinopathies are caused by one, or a combination, of abnormal haemoglobins which cause the red blood cell to adopt an anomalous shape under conditions of hypoxia and acidosis. Because these deformed red blood cells are more rigid than healthy cells, they may become impacted in and obstruct small blood vessels, causing tissue ischaemia with a marked local increase in acidosis and hypoxia, and even more sickling. The sickling disorders in which the mutant haemoglobins S and C are inherited as alleles of normal haemoglobin A have important ocular manifestations. These abnormal haemoglobins may occur in combination with normal haemoglobin A or in association with each other as indicated below:

1. **AS** (sickle-cell trait) is present in 8% of African Americans. It is the mildest form and usually requires

severe hypoxia or other abnormal conditions to produce sickling.

2. **SS** (sickle-cell disease, sickle-cell anaemia) is present in 0.4% of African Americans. It causes severe systemic complications, such as painful infarctive crises and severe haemolytic anaemia. Ocular complications are usually mild and asymptomatic.
3. **SC** (sickle-cell C disease) is present in 0.2% of African Americans.
4. **SThal** (sickle-cell thalassaemia); both SC and SThal are associated with mild anaemia but severe ocular manifestations.

Proliferative retinopathy

Although the most severe forms of retinopathy are associated with SC and SThal diseases, SS may occasionally also cause retinopathy.

Clinical features

1. **Staging** (Fig. 14.91)
   - *Stage* 1. Peripheral arteriolar occlusion.
   - *Stage* 2. Peripheral arteriovenous anastomoses which appear to be dilated pre-existent capillary channels. The peripheral retina beyond the point of vascular occlusion is largely avascular and non-perfused.
   - *Stage* 3. Sprouting of new vessels from the anastomoses. Initially, the new vessels lie flat on the retina, have a 'sea-fan' configuration and are usually fed by a single arteriole and drained by a single vein (Fig. 14.92a). Between 40% and 50% of 'sea-fans' spontaneously involute as a result of auto-infarction and appear as greyish fibrovascular lesions. In other cases the neovascular tufts continue to proliferate, become adherent to the cortical vitreous gel and may bleed as a result of vitreoretinal traction (Fig. 14.93).
   - *Stage* 4. Vitreous haemorrhage which may be precipitated by relatively trivial ocular trauma.
   - *Stage* 5. Extensive fibrovascular proliferation and tractional retinal detachment (Fig. 14.94). Rhegmatogenous retinal detachment may also occur as a result of tear formation adjacent to areas of fibrovascular tissue.
2. **FA** shows extensive capillary non-perfusion of the peripheral retina (*see* Fig. 14.92b) and late leakage from neovascularization (*see* Fig. 14.92c).

Treatment

1. **Peripheral retinal photocoagulation** to areas of capillary non-perfusion may be required to induce regression of neovascular tissue in patients with recurrent vitreous haemorrhages. However, unlike DR, new vessels in sickle cell disease tend to auto-infarct and involute spontaneously without treatment.
2. **Pars plana vitrectomy** for tractional retinal detachment and/or persistent vitreous haemorrhage usually gives poor results.

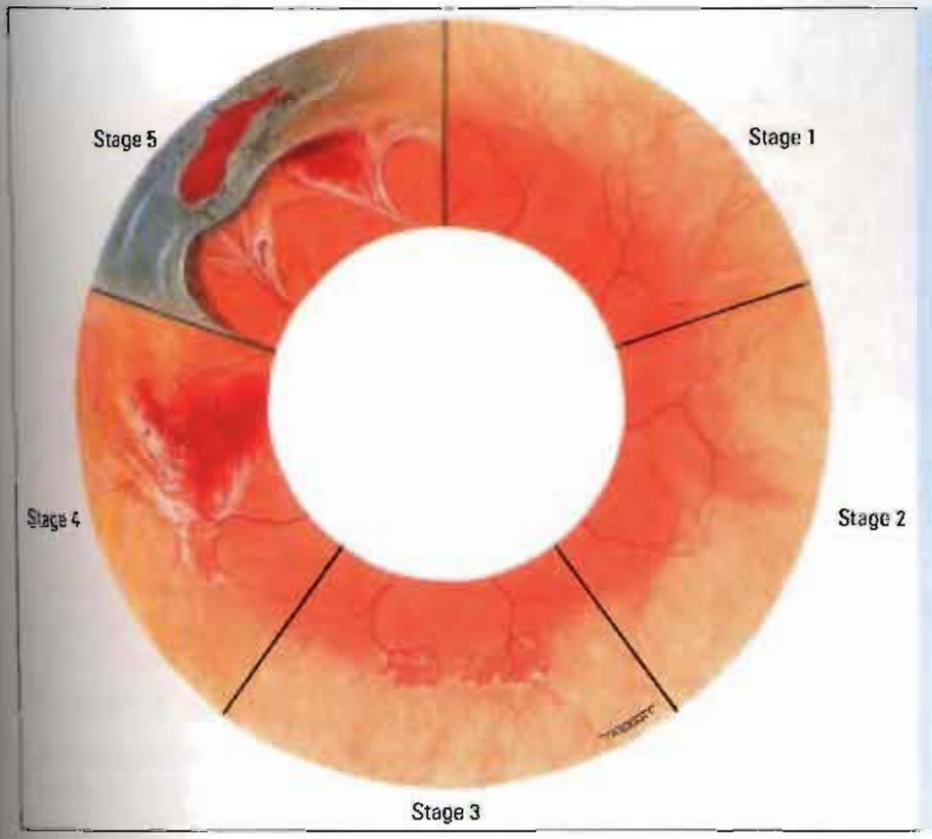
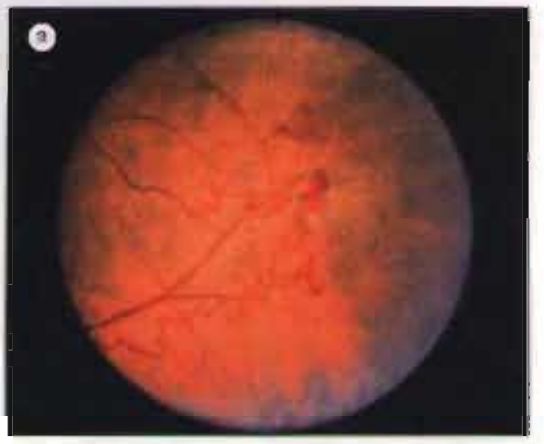


Fig. 14.91
Grading of proliferative sickle-cell retinopathy (*see text*)



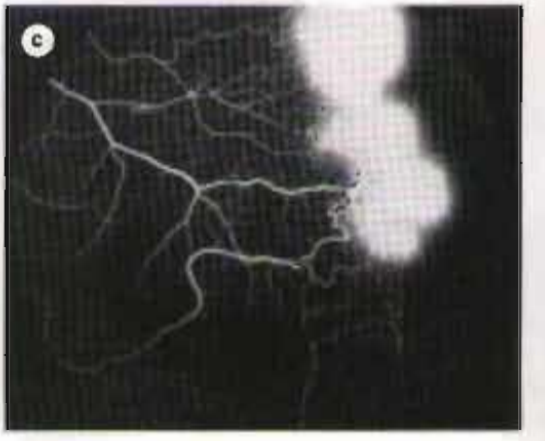


Fig. 14.92
(a) Proliferative sickle-cell retinopathy stage 3; (b) early FA showing filling of new vessels ('sea-fans') and extensive peripheral retinal capillary non-perfusion; (c) late FA showing leakage from new vessels.

Fig. 14.93
Haemorrhage from new vessels in stage 4 proliferative sickle-cell retinopathy.

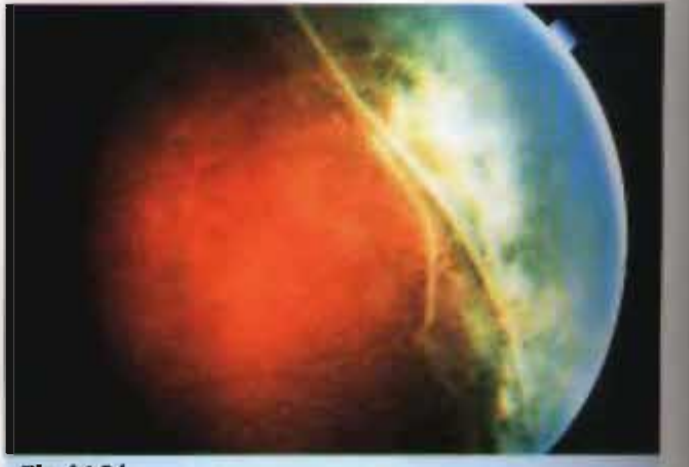


Fig. 14.94
Peripheral tractional retinal detachment in stage 5 proliferative sickle-cell retinopathy.

Non-proliferative retinopathy

Asymptomatic lesions

1. **Venous tortuosity** is one of the first ophthalmic signs of sickling and is due to peripheral arteriovenous shunts.
2. **Silver-wiring of arterioles** in the peripheral retina, which represent previously occluded arterioles.
3. **Salmon patches** are pink, preretinal (Fig. 14.95) or superficial intraretinal haemorrhages at the equator, which lie adjacent to arterioles and usually resolve without sequelae.
4. **Black sunbursts** are patches of peripheral RPE hyperplasia (Fig. 14.96).
5. **Macular depression sign** is an oval depression of the bright central macular reflex due to atrophy and thinning of the sensory retina.

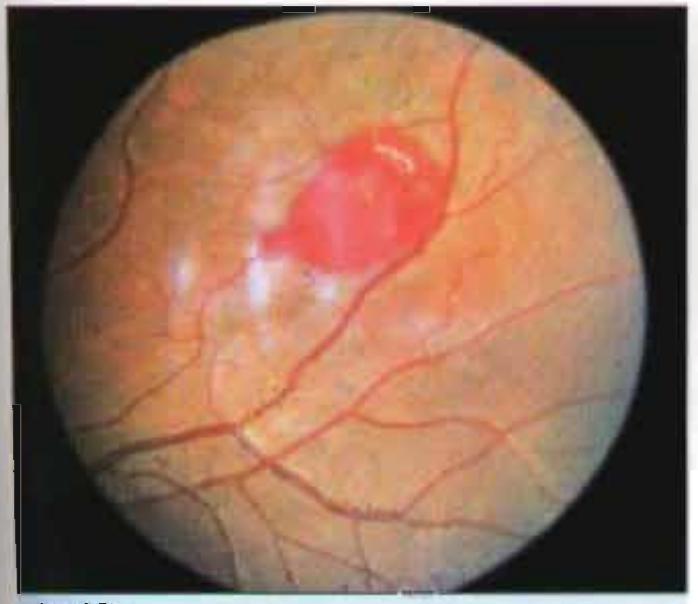


Fig. 14.95
Preretinal haemorrhage (salmon patch) in sickle-cell retinopathy

Fig. 14.96
Peripheral RPE hyperplasia (black sunburst) in sickle-cell retinopathy

6. **Peripheral retinal holes** and areas of whitening similar to 'white-without-pressure' are occasionally seen (Fig. 14.97).

Symptomatic lesions

1. **Macular arteriolar occlusion** occurs in about 30% of patients.
2. **Acute CRAO** is rare.

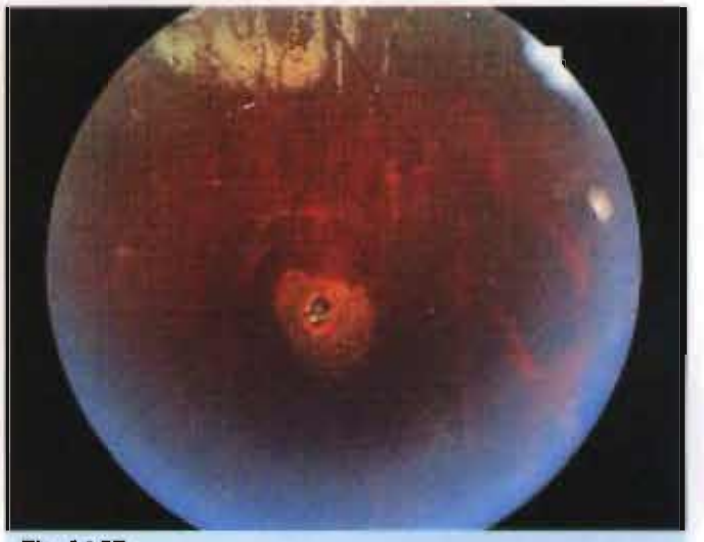


Fig. 14.97
Peripheral retinal hole and an area of whitening superiorly in sickle-cell retinopathy

3. **Retinal vein occlusion**, due to hyperviscosity, is uncommon.
4. **Choroidal vascular occlusion** may be seen occasionally, particularly in children.
5. **Angioid streaks** occur in a minority of patients.

Non-retinal lesions

1. **Conjunctival** lesions are characterized by isolated dark-red vascular anomalies shaped like commas or corkscrews. They involve the small calibre vessels and are most often located inferiorly.
2. **Iris** lesions consist of circumscribed areas of ischaemic atrophy, usually at the pupillary edge and extending to the collarette. Rubeosis may be seen occasionally.

Retinopathy of prematurity

Introduction

Retinopathy of prematurity (ROP) is a proliferative retinopathy affecting pre-term infants of low birth weight who have often been exposed to high ambient oxygen concentrations. The retina is unique among tissues in that it has no blood vessels until the fourth month of gestation, at which time vascular complexes emanating from the hyaloid vessels at the optic disc grow towards the periphery. These vessels reach the nasal periphery after 8 months of gestation, but do not reach the temporal periphery until about 1 month after delivery. The incompletely vascularized temporal retina is particularly susceptible to oxygen damage, especially in the pre-term infant.

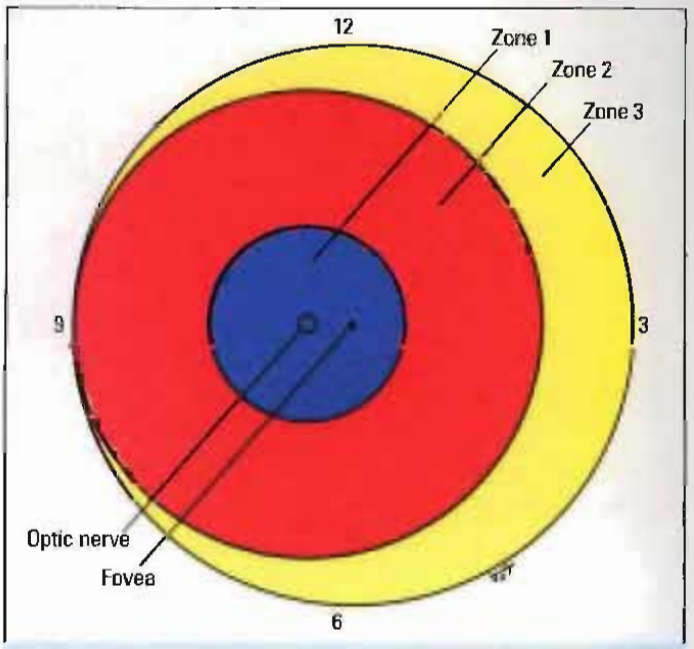


Fig. 14.98
Grading of retinopathy of prematurity (see *text*)

Active ROP

Severity

This is determined in terms of (a) *location*, (b) *extent*, (c) *stages* and (d) *'plus' disease* as follows:

1. **Location** is determined according to three zones centred on the optic disc (Fig. 14.98).
   - *a. Zone 1* is bounded by an imaginary circle the radius of which is twice the distance from the disc to the macula.
   - *b. Zone 2* extends concentrically from the edge of zone 1 to the nasal ora serrata and to an area near the temporal equator.
   - *c. Zone 3* consists of a residual temporal crescent anterior to zone 2.
2. **Extent** of involvement is determined by the number of clock hours of retina involved.
3. **Staging**
   - *a. Stage 1* (demarcation line). The first pathognomonic sign of ROP is the development of a thin, tortuous, grey-white line running roughly parallel with the ora serrata which

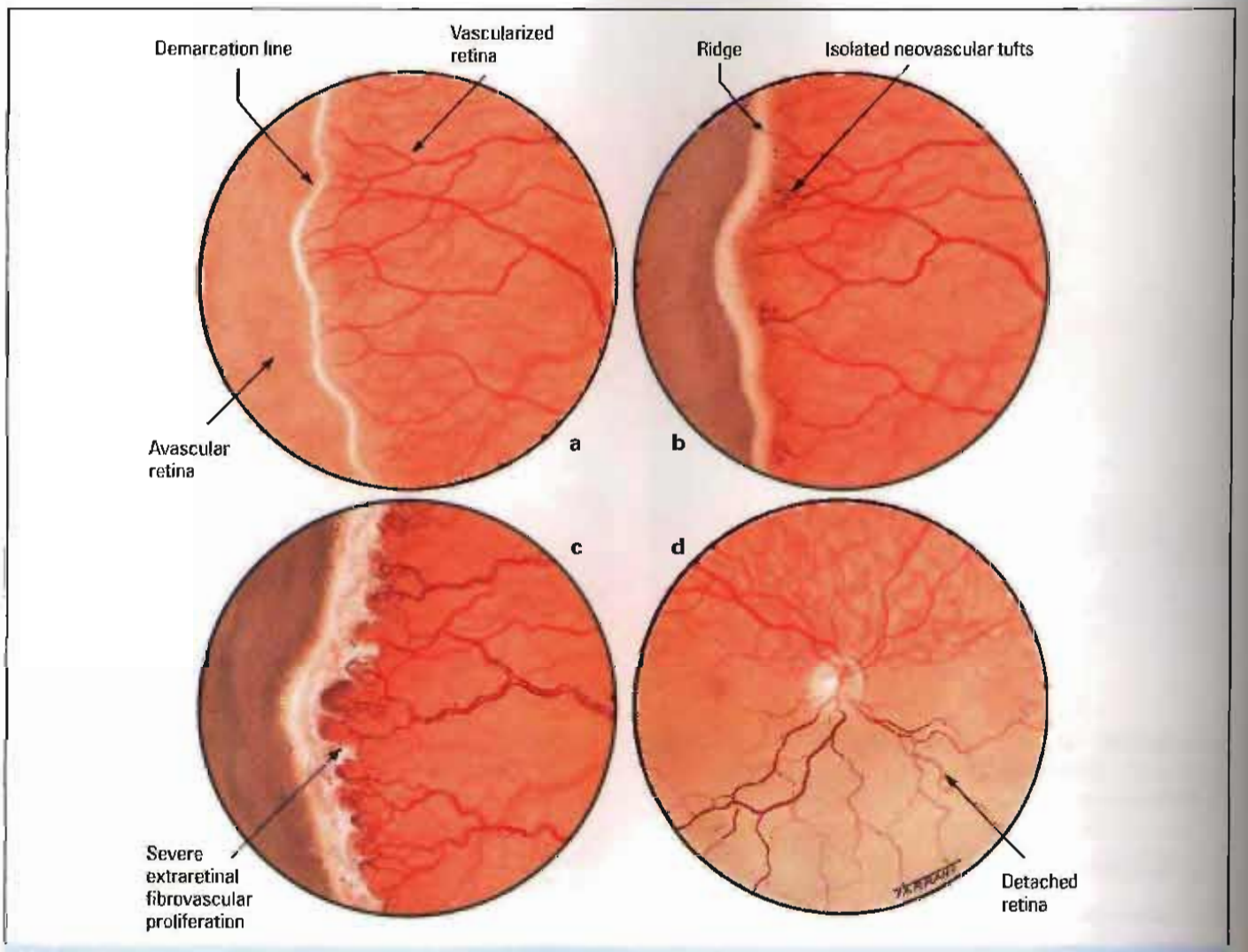


Fig. 14.99
Progression of retinopathy of prematurity (see *text*)

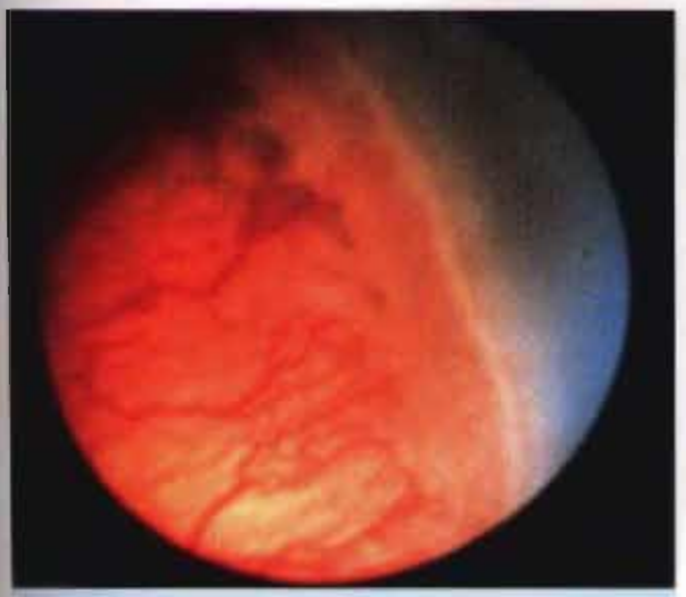


Fig. 14.100
Elevated ridge in retinopathy of prematurity stage 2 (Courtesy of J Arnold)

Fig. 14.101
Ridge with extensive fibrovascular proliferation in retinopathy of prematurity stage 3

separates avascular immature peripheral retina from vascularized posterior retina (Fig. 14.99a). The line is more prominent in the temporal periphery and may have abnormal branching blood vessels leading up to it.

b. *Stage 2* (ridge). If ROP progresses the demarcation line develops into an elevated ridge which represents a mesenchymal shunt joining arterioles with veins (Figs 14.99b and 14.100). Blood vessels enter the ridge and small isolated neovascular tufts may be seen posterior to it.

c. *Stage 3* (ridge with extraretinal fibrovascular proliferation). As the disease progresses, the ridge develops a pink colour due to fibrovascular proliferation which grows along the surface of the retina and into the vitreous (Figs 14.99c and 14.101). This is often associated with dilatation and tortuosity of the retinal blood vessels posterior to the equator. Retinal haemorrhage is common, and vitreous haemorrhage may develop. The highest incidence of this stage is around the post-conceptual age of 35 weeks.

d. *Stage 4* (sub-total retinal detachment) is due to progressive fibrovascular proliferation (Fig. 14.99d). The detachment, which starts in the extreme periphery and then spreads centrally, typically develops when the infant is about 10 weeks old.

e. *Stage 5* is a total retinal detachment.

> ***NB:*** Although the clinical features of ROP usually take several weeks to develop, rarely the disease can progress from stage 1 to stage 4 within a few days. In about 80% of infants, ROP regresses spontaneously, leaving few if any residua. Spontaneous regression may even occur in patients with partial retinal detachments.

Other considerations

1. **Plus disease** signifies a tendency to progression and is characterized by the following:
   - Failure of the pupil to dilate, associated with gross vascular engorgement of the iris.
   - Development of vitreous haze.
   - Dilatation of veins and tortuosity of the arteries in the posterior fundus (Fig. 14.102).
   - Increasing preretinal and vitreous haemorrhage.

   When these changes are present, a plus sign is added to the stage number.
2. **Threshold disease** is defined as five contiguous clock hours or eight non-contiguous clock hours of extraretinal neovascularization (stage 3 disease) in zone 1 or zone 2, associated with plus disease, and is an indication for treatment.

Screening

Babies born at or before 31 weeks gestational age, or weighing 1500 g or less, should be screened for ROP.

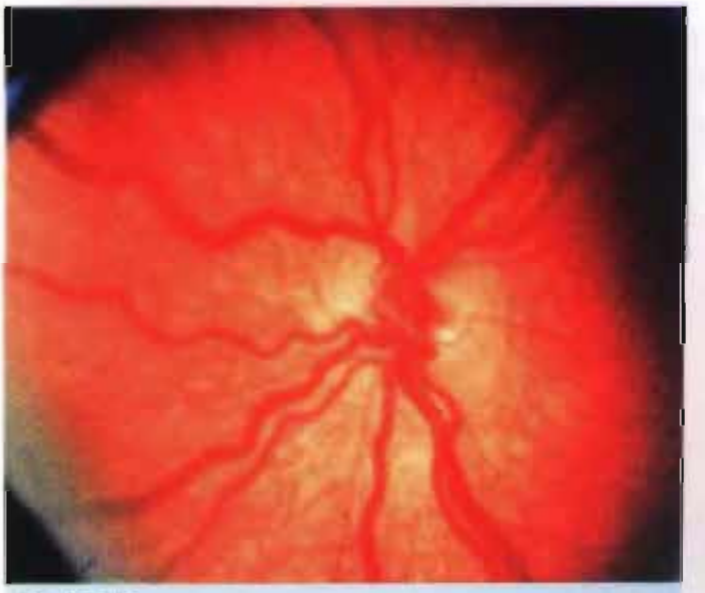


Fig. 14.102
Vascular dilatation in retinopathy of prematurity 'plus' disease

Fig. 14.103
Peripheral fibrous proliferation and pigmentary changes with straightening of temporal blood vessels in cicatricial retinopathy of prematurity

Screening prior to the age of 31 weeks gestational age is, however, often of little value since pupillary dilatation is difficult and visualization of the fundus is impaired by the tunica vasculosa lentis. Screening of premature infants should therefore be between 6 and 7 weeks post-natal age or 34 weeks post-conceptual age (whichever comes first), but not before 5 weeks post-natal age, to detect the onset of threshold disease. Subsequent review should be at 2-weekly intervals, until retinal vascularization reaches zone 3. Other systemic complications, such as intraventricular haemorrhage, may increase the risk of ROP. The pupils in a pre-term infant should be dilated with 0.5% cyclopentolate with or without 2.5% phenylephrine.

Treatment

1. **Ablation** of avascular immature retina by cryotherapy or laser photocoagulation is recommended in infants with threshold disease. This is successful in 85% of cases, but the remainder progress to retinal detachment in spite of treatment.
2. **Vitreoretinal surgery** for tractional retinal detachment usually has a poor visual outcome.

Cicatricial ROP

About 20% of infants with active ROP develop cicatricial complications, which range from innocuous to extremely severe. In general, the more advanced or the more posterior the proliferative disease at the time of involution, the worse the cicatricial sequelae.

- **Stage 1.** Myopia associated with mild peripheral retinal pigmentary disturbance and haze at the vitreous base.
- **Stage 2.** Temporal vitreoretinal fibrosis (Fig. 14.103) with dragging of the macula (Fig. 14.104), which may lead to a pseudo-exotropia, due to resultant exaggeration of angle kappa (*see* Chapter 16).
- **Stage 3.** More severe peripheral fibrosis with contracture and a falciform retinal fold (Fig. 14.105).
- **Stage 4.** Partial ring of retrolental fibrovascular tissue with partial retinal detachment.
- **Stage 5.** Complete ring of retrolental fibrovascular tissue with total retinal detachment (Fig. 14.106), a picture formerly known as 'retrolental fibroplasia'. Secondary angle-closure glaucoma may develop due to progressive

Fig. 14.104
Temporal dragging of the macula in cicatricial retinopathy of prematurity

Fig. 14.105
Falciform vitreoretinal fold with inferotemporal dragging of the retina in cicatricial retinopathy of prematurity

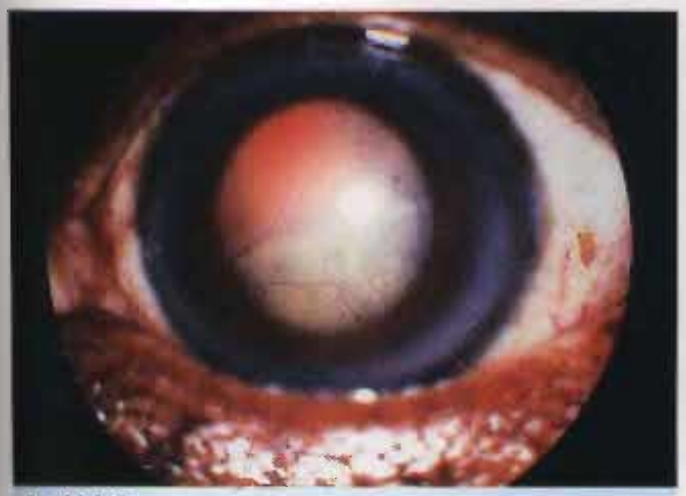


Fig. 14.106
Total retinal detachment in retinopathy of prematurity

Fig. 14.107
Retinal artery macroaneurysm with localized haemorrhage

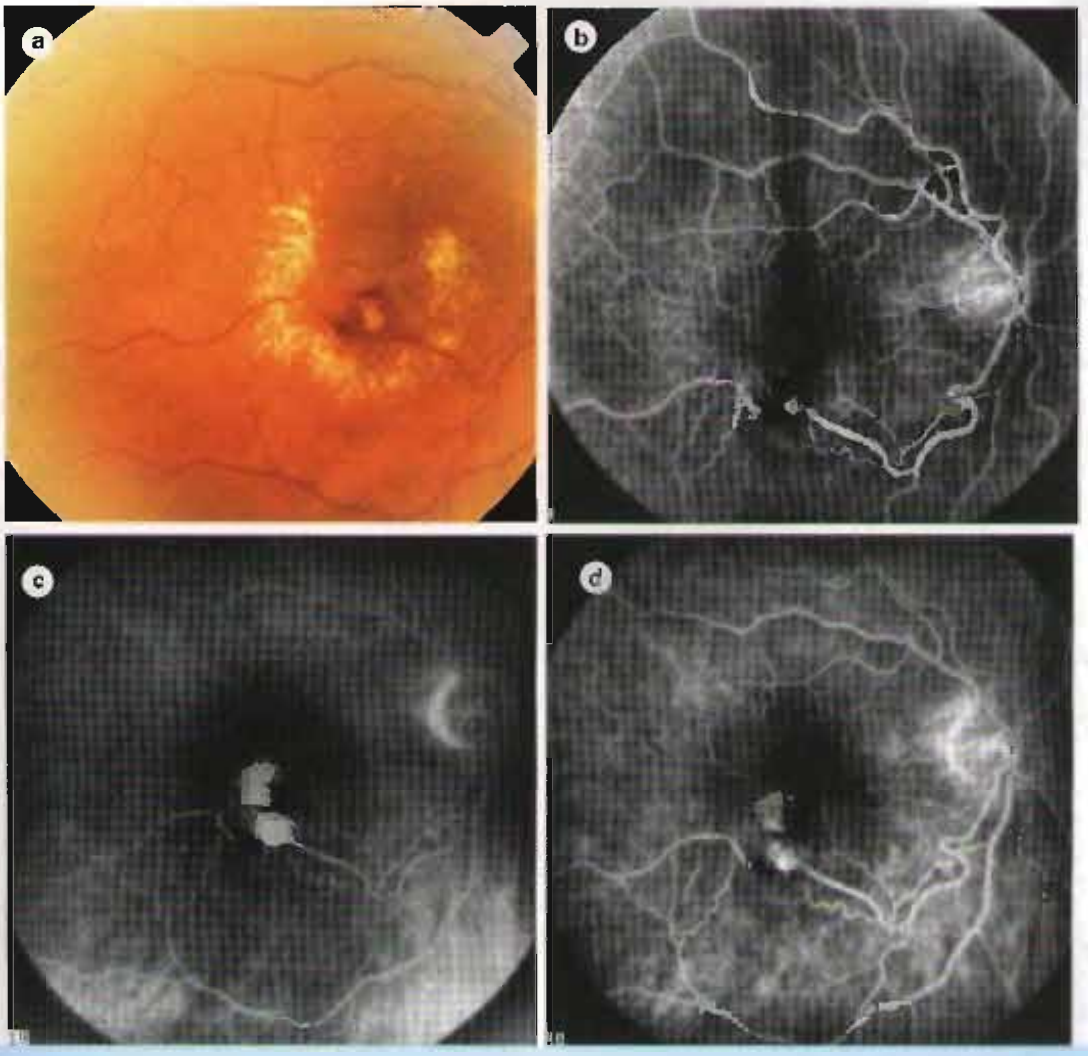


Fig. 14.108
(a) Leaking retinal artery macroaneurysm with a small haemorrhage and surrounding hard exudates; (b) early venous phase FA showing filling; (c) late venous phase showing late leakage; (d) late phase showing further leakage (Courtesy of S. Milewski)

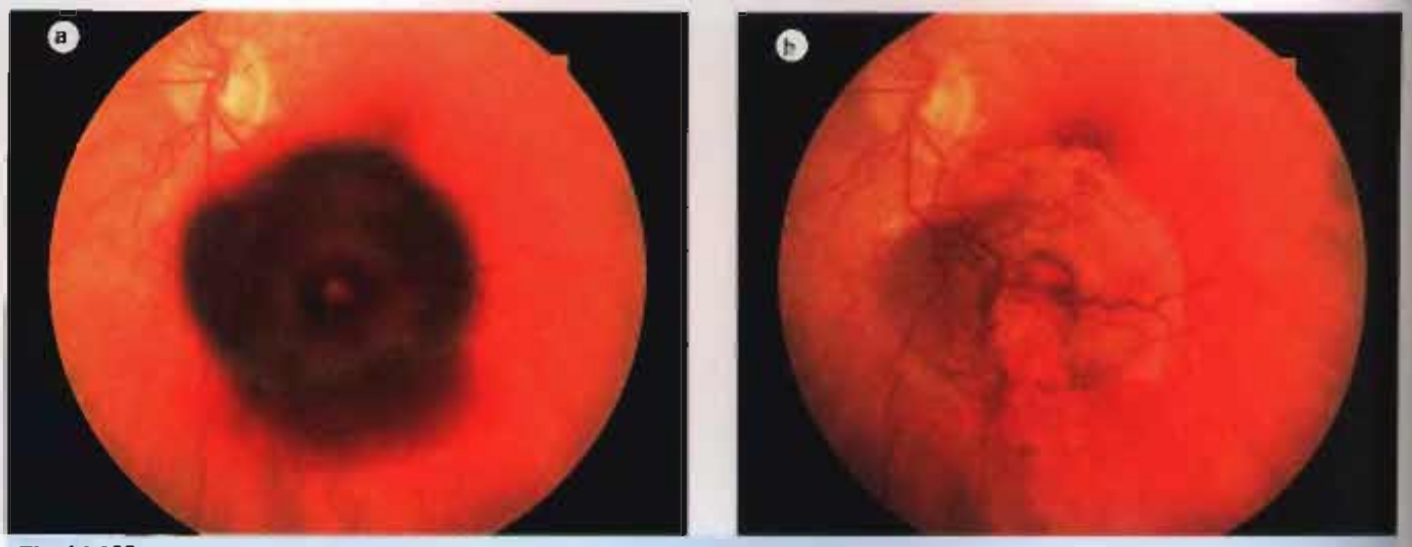


Fig. 14.109
(a) Subretinal haemorrhage associated with retinal artery macroaneurysm; (b) following spontaneous involution and absorption of blood

shallowing of the anterior chamber caused by a forward movement of the iris–lens diaphragm and the development of anterior synechiae. Treatment is by lensectomy and anterior vitrectomy.

Retinal artery macroaneurysm

A retinal artery macroaneurysm is a localized dilatation of a retinal arteriole which usually occurs in the first three orders of the arterial tree. It has a predilection for elderly hypertensive women and involves one eye in 90% of cases.

Clinical features

1. **Presentation** may be in one of the following ways:
   - Detection by chance of an asymptomatic lesion.
   - Insidious impairment of central vision due to macular oedema and hard exudate formation.
   - Sudden visual loss resulting from vitreous haemorrhage is uncommon.
2. **Fundus**
   - A saccular or fusiform arteriolar dilatation, most frequently occurring at a bifurcation or an arteriovenous crossing along the temporal vascular arcades. The aneurysm may enlarge to several times the diameter of the artery.
   - Associated retinal haemorrhage is present in 50% of cases (Fig. 14.107).
   - Multiple macroaneurysms along the same or different arterioles may be present.
3. **FA** findings are dependent on the patency of the lesion and any associated haemorrhage. The typical appearance is that of early uniform filling of the macroaneurysm (Fig. 14.108b) with late leakage (Fig. 14.108c and d). Incomplete filling is due to partial or complete obliteration of the lumen by thrombosis.
4. **Course**
   - Spontaneous involution following thrombosis and fibrosis is very common. This may precede or follow the development of leakage or haemorrhage (Fig. 14.109).
   - Rupture with haemorrhage (Fig. 14.110), which may be subretinal, intraretinal, preretinal or vitreous. In these cases the underlying lesion may be overlooked and the diagnosis missed.
   - Chronic leakage resulting in retinal oedema with accumulation of hard exudates at the fovea is common and may result in permanent loss of central vision (*see* Fig. 14.108a).

Management

1. **Observation** in anticipation of spontaneous involution is indicated in eyes with good visual acuity in which

Fig. 14.110
Subretinal and preretinal haemorrhage associated with a retinal artery macroaneurysm (Courtesy of S. Milewski)

the macula is not threatened and those with mild retinal haemorrhage without significant oedema or exudation.

2. **Argon laser photocoagulation** may be considered if oedema or hard exudates threaten or involve the fovea (Fig. 14.111a), particularly if there is documented visual deterioration. The burns may be applied to the lesion itself, the surrounding area, or both (Fig. 14.111b). It may take several months for the oedema and hard exudates to absorb.
3. **YAG-laser hyaloidotomy** may be considered in eyes with large non-absorbing preretinal haemorrhages overlying the macula in order to disperse the blood into the vitreous cavity, from where it may be absorbed more quickly.

Differential diagnosis

1. **Hard exudates at the posterior pole**
   - Background diabetic retinopathy.
   - Exudative age-related macular degeneration.
   - Old retinal branch vein occlusion.
   - Retinal telangiectasia.
   - Small retinal capillary haemangioma.
   - Radiation retinopathy.
2. **Deep retinal or subretinal haemorrhages at the posterior pole**
   - Choroidal neovascularization.
   - Valsalva retinopathy.
   - Idiopathic polypoidal choroidal vasculopathy.
   - Blunt ocular trauma.
   - Choroidal melanoma
   - Terson syndrome associated with subarachnoid haemorrhage.

Primary retinal telangiectasia

The primary retinal telangiectasias are a group of rare, idiopathic, congenital or acquired, retinal vascular anomalies characterized by dilatation and tortuosity of retinal blood vessels, multiple aneurysms, vascular leakage and the deposition of hard exudates. Retinal telangiectasias involve the capillary bed, although the arterioles and venules may also be involved. The vascular malformations often progress and become symptomatic later in life as a result of haemorrhage, oedema or lipid exudation. Primary and secondary telangiectasias should be distinguished from each other, the latter being associated with an underlying systemic disease, such as diabetes. According to severity primary retinal telangiectasias can be divided into: (a) *idiopathic juxtafoveolar retinal telangiectasia*, (b) *Leber miliary aneurysms* and (c) *Coats disease*. Some authorities consider Leber miliary aneurysms to be a localized and milder form of Coats disease.

Idiopathic juxtafoveolar retinal telangiectasia

Idiopathic juxtafoveolar telangiectasia is a rare, congenital or acquired condition which can be divided into the following types.

Group 1A: unilateral parafoveal telangiectasia

This typically affects middle-aged men.

1. **Presentation** is with mild to moderate blurring of vision.

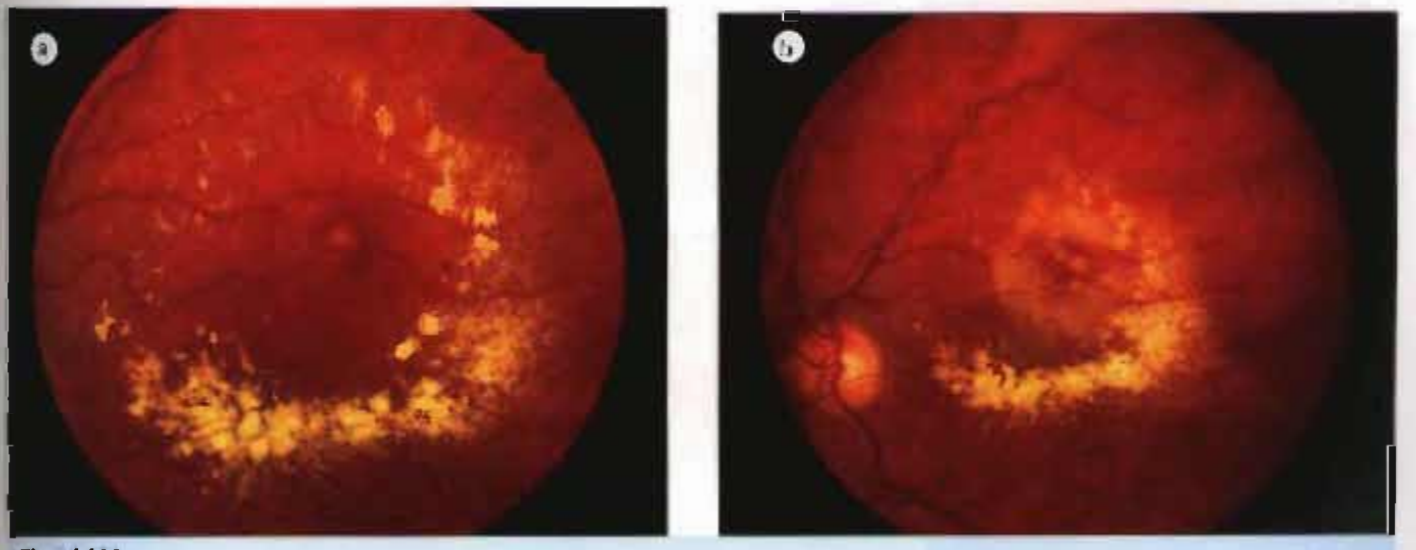


Fig. 14.111
(a) Leaking retinal artery macroaneurysm with hard exudates involving the fovea; (b) appearance immediately following laser photocoagulation

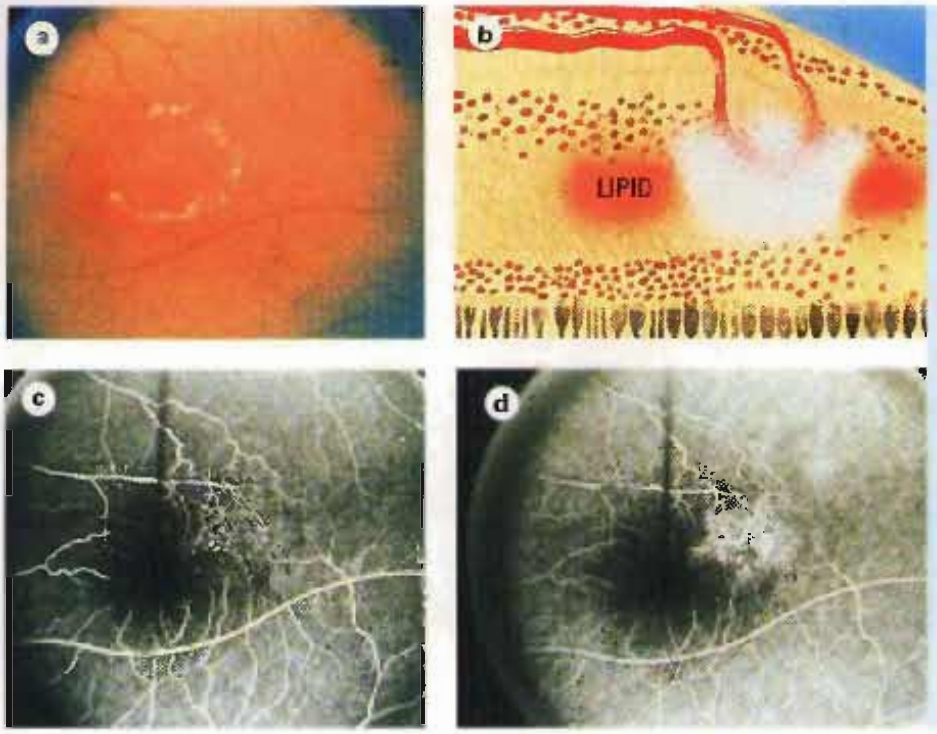


Fig. 14.112
Idiopathic juxtafoveolar retinal telangiectasia: group **1A** (see *text*) (Courtesy of Wilmer Institute)

2. **Signs**. Telangiectasia, about 1.5 disc diameters in area, temporal to the fovea and frequently associated with hard exudates (Fig. 14.112a and b).
3. **FA** shows capillary dilatation (Fig. 14.112c) and late leakage (Fig. 14.112d).
4. **Treatment** by laser photocoagulation to areas of leakage may be beneficial in preventing visual loss.

Group 1B: unilateral parafoveal telangiectasia

This typically affects middle-aged men.

1. **Presentation** is with mild blurring of vision.
2. **Signs**. Telangiectasia confined to one clock hour at the edge of FAZ (Fig. 14.113a and b).
3. **FA** shows absence of leakage (Fig. 14.113c).
4. **Treatment** is not appropriate and the prognosis is good

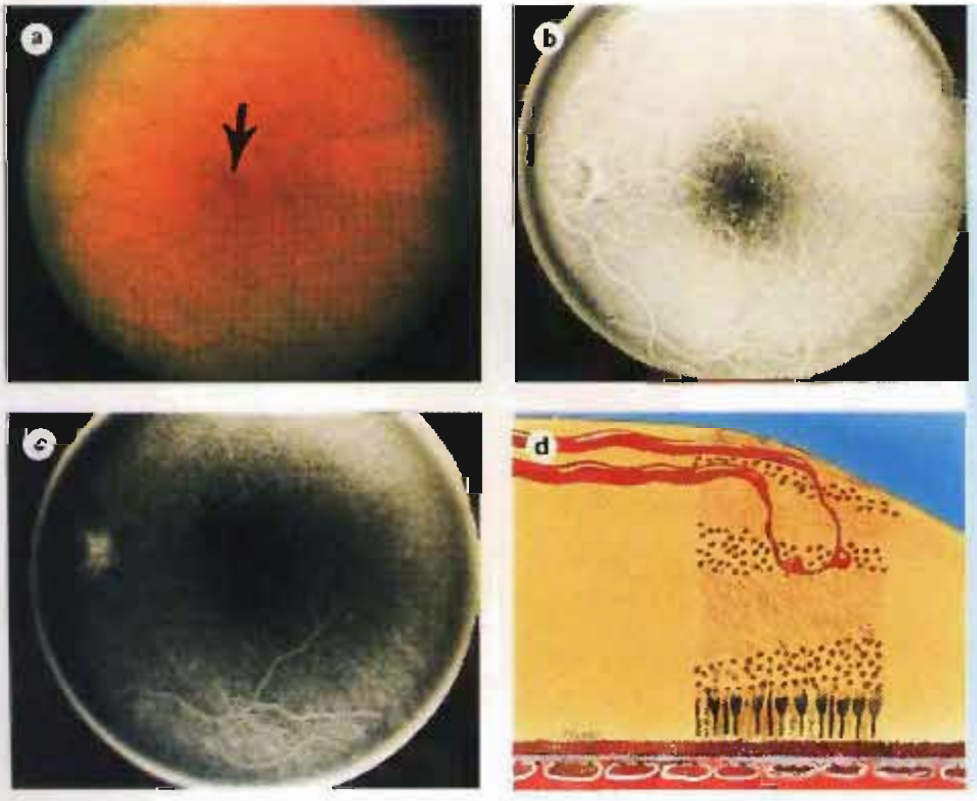


Fig. 14.113
Idiopathic juxtafoveolar retinal telangiectasia: group **1B** (see *text*) (Courtesy of Wilmer Institute)

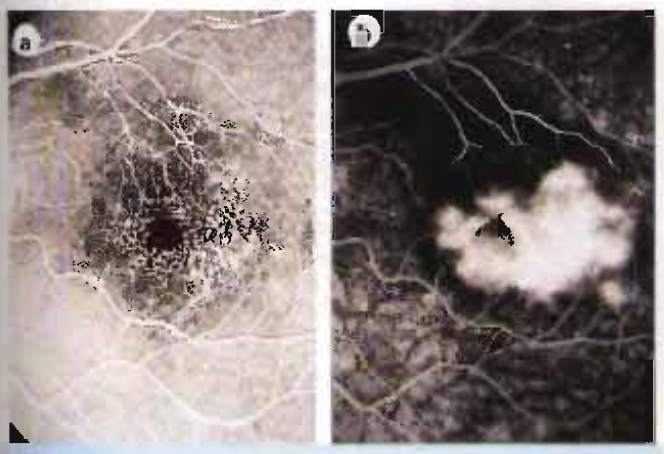


Fig. 14.114
Idiopathic juxtafoveolar retinal telangiectasia: group 2 (see text)

Group 2: bilateral parafoveolar telangiectasia

1. **Presentation** is in the fifth to sixth decades with mild, slowly progressive disturbance of central vision.
2. **Signs**
   - Symmetrical telangiectasia, one disc area or less, involving all or a part of the parafoveolar retina without hard exudates but frequently associated with stellate plaques of RPE hyperplasia.
   - Multiple glistening white juxtafoveolar dots and solitary small yellow central deposits may be present.
3. **FA** shows capillary dilatation outside the FAZ (Fig. 14.114a) and late leakage (Fig. 14.114b).
4. **Prognosis** is guarded because of the development of secondary foveal atrophy and occasionally CNV. Laser photocoagulation may be of benefit in patients with CNV but not otherwise.

Group 3: bilateral perifoveal telangiectasia and capillary occlusion

This is the most severe form and typically presents in the sixth decade.

1. **Presentation** is with slowly progressive loss of central vision.
2. **Signs**
   - Marked aneurysmal dilatation of terminal capillaries and progressive occlusion of perifoveal capillaries.
   - Optic atrophy may be present.
3. **FA** shows widening of FAZ but absence of leakage.
4. **Prognosis** is usually poor.

Leber miliary aneurysms

1. **Presentation** is in adult life with unilateral impairment of central vision.
2. **Signs**
   - Fusiform and saccular dilatation of venules and arterioles, most commonly involving the temporal retinal periphery (Fig. 14.115).

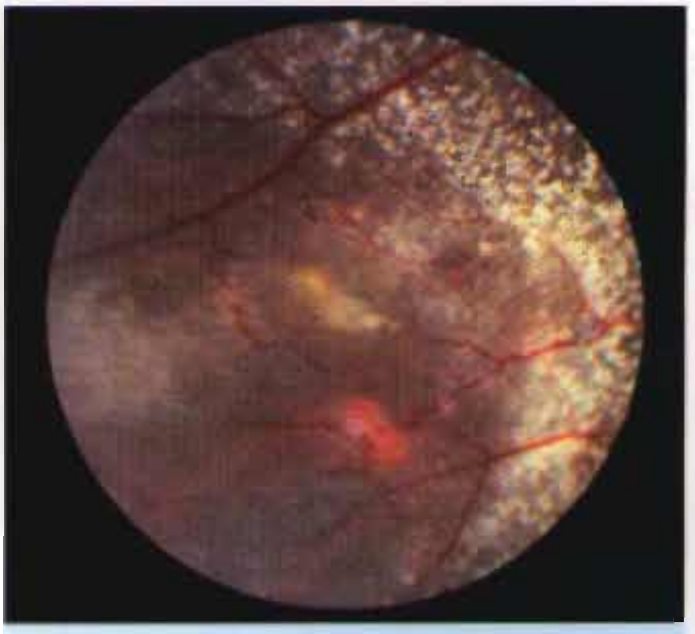


Fig. 14.115
Peripheral lesions in Leber miliary aneurysms

   - Chronic leakage results in intraretinal hard exudate formation which may involve the macula.
3. **FA** during the early phase highlights the vascular anomalies and shows areas of retinal non-perfusion (Fig. 14.116b). The late phase shows leakage (Fig. 14.116c).
4. **Prognosis** is dependent on the extent of foveal involvement by hard exudates at the time of diagnosis (Fig. 14.117a).
5. **Treatment** to ablate the vascular anomalies by photocoagulation may be beneficial if applied early (Fig. 14.117b).

Coats disease

Coats disease is the most severe form of retinal telangiectasia. It is usually unilateral, typically affects young boys and can cause severe visual loss from exudative retinal detachment.

Clinical features

1. **Presentation** is typically in the first decade (average 5 years) with visual loss, strabismus or a white fundus reflex (leukocoria) (Fig. 14.118).
2. **Signs** (in chronological order)
   - Retinal telangiectasia, most often in the inferior and temporal quadrants between the equator and ora serrata, and sometimes posterior to the equator towards the vascular arcades (Fig. 14.119).
   - Intraretinal and subretinal yellowish exudation (Figs 14.120 and 14.121a) often affecting areas remote from the vascular abnormalities, particularly the macula.

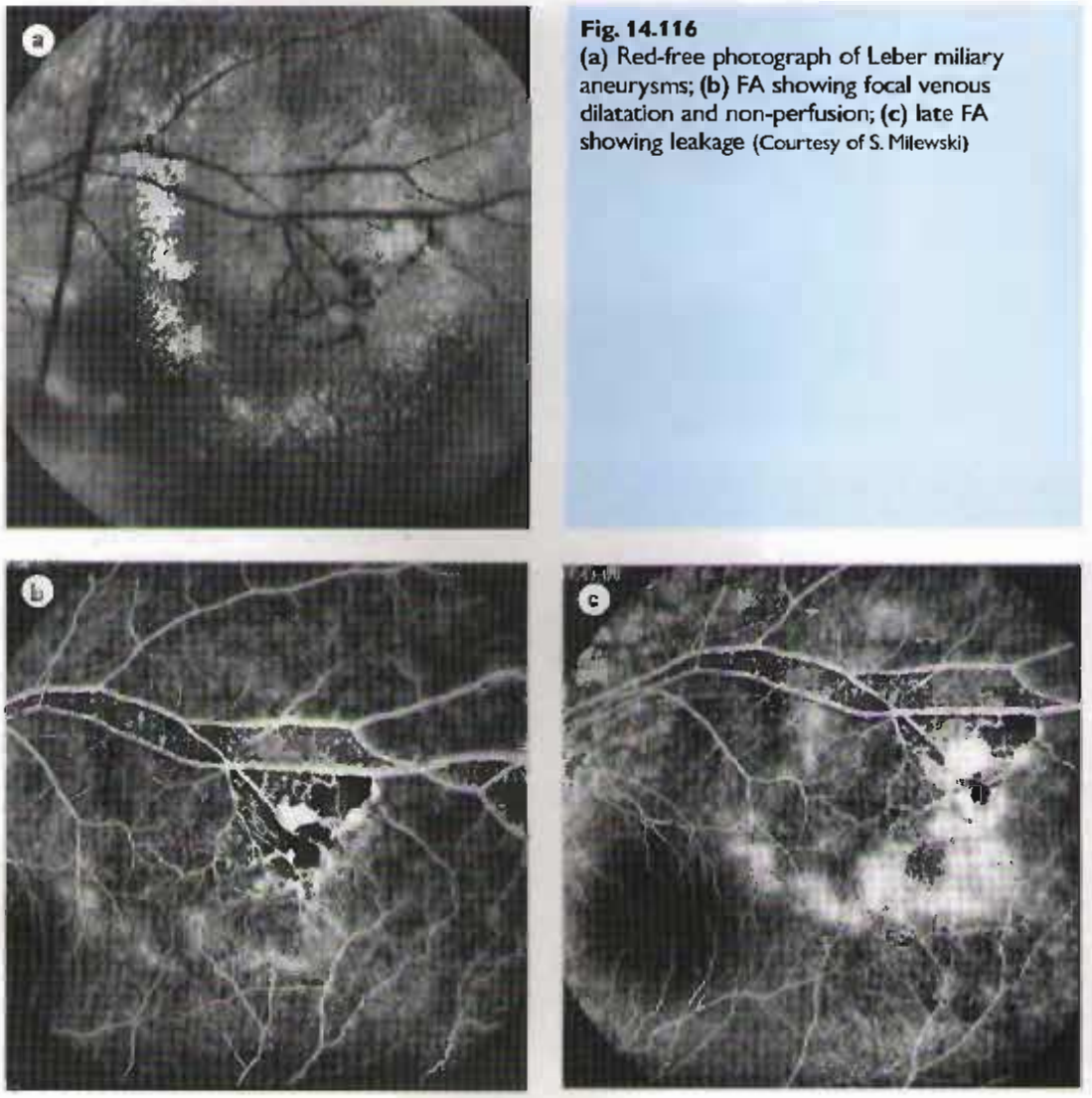


Fig. 14.116
(a) Red-free photograph of Leber miliary aneurysms; (b) FA showing focal venous dilatation and non-perfusion; (c) late FA showing leakage (Courtesy of S. Milewski)

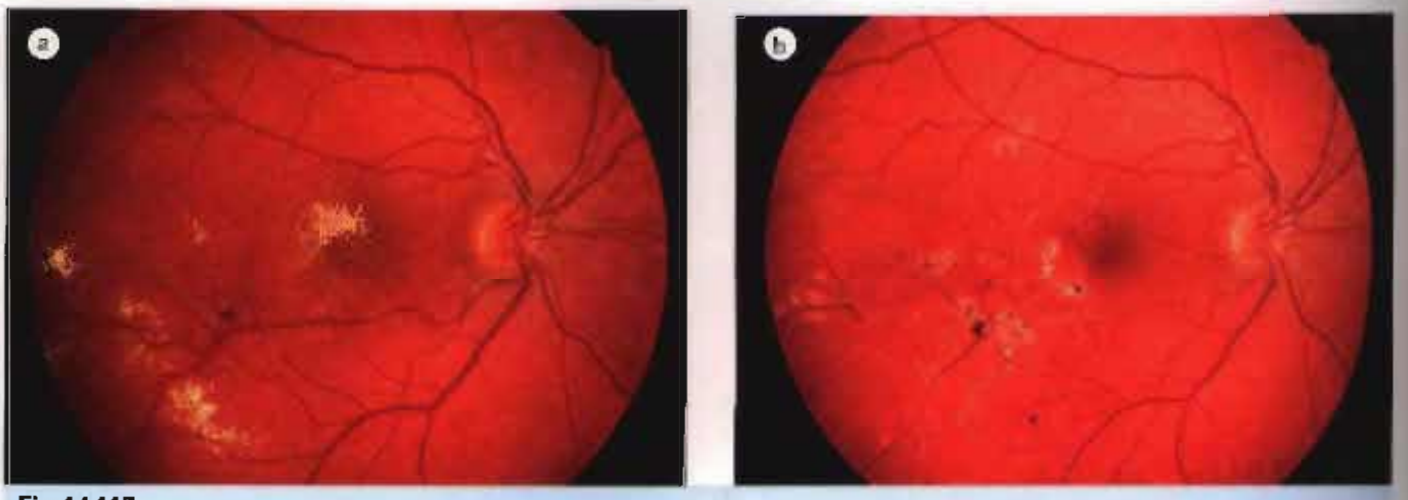


Fig. 14.117
(a) Hard exudates in Leber miliary aneurysms; (b) absorption of hard exudates following laser photocoagulation (Courtesy of S. Milewski)

Fig. 14.118
White pupil (leukocoria) in advanced Coats disease

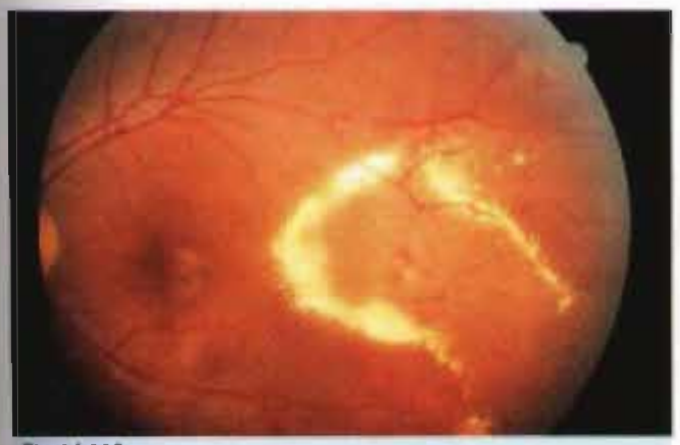


Fig. 14.119
Vascular changes and exudates in early Coats disease

3. **Complications** include exudative retinal detachment, rubeosis iridis, glaucoma, uveitis and phthisis bulbi.
4. **FA** highlights the underlying telangiectasia. Tortuosity, aneurysm formation and non-perfusion are seen with variable blockage of background choroidal fluorescence by hard exudates (Fig. 14.121b).
5. **Ultrasonography** in eyes with total retinal detachment is useful to exclude exophytic retinoblastoma.
6. **Differential diagnosis** includes other causes of unilateral leukocoria and retinal detachment in children such as late-onset retinoblastoma, toxocariasis, incontinentia pigmenti and retinal capillary haemangioma.

Management

1. **Observation** in patients with mild, non-vision-threatening disease and in those with a comfortable eye with total retinal detachment in which there is no hope of restoring useful vision.
2. **Photocoagulation** to areas of telangiectasia in eyes with exudation but no or very shallow retinal detachment.
3. **Cryotherapy**, with a double freeze–thaw method, when retinal detachment is shallow enough to allow approximation of the cryoprobe to the telangiectasia.
4. **Vitreoretinal surgery** in eyes with deep retinal detachments unsuitable for cryotherapy.

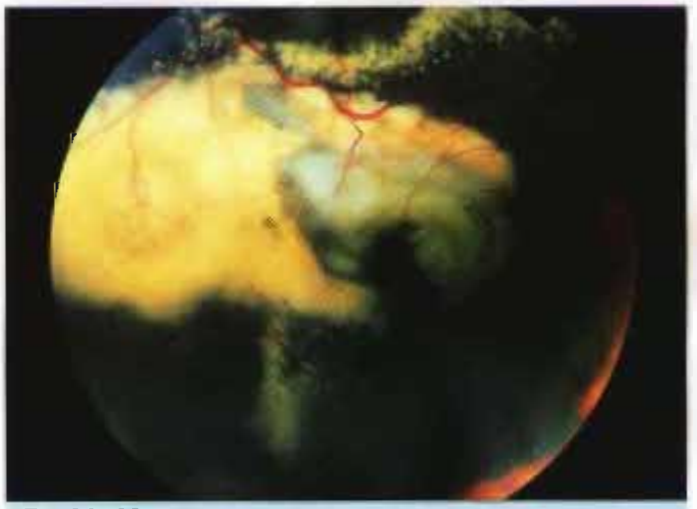


Fig. 14.120
Extensive subretinal exudation in advanced Coats disease

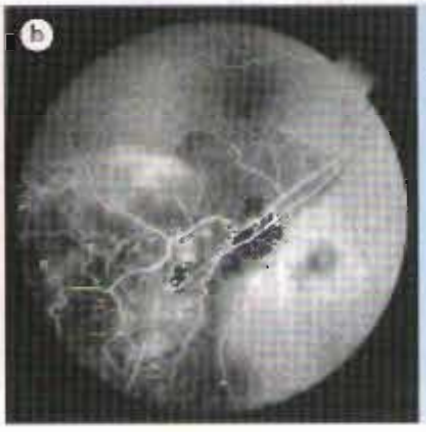


Fig. 14.121
(a) Coats disease; (b) FA showing vascular abnormalities and blockage of background fluorescence by hard exudates (Courtesy of S. Milewski)

Radiation retinopathy

Radiation retinopathy may develop following treatment of intraocular tumours by plaque therapy (brachytherapy) or external beam irradiation of sinus, orbital or nasopharyngeal malignancies.

1. **Presentation**. The time interval between exposure and disease is variable and unpredictable, although commonly between 6 months and 3 years.
2. **Signs** (in chronological order)
   - Discrete capillary occlusion with the development of collateral channels and microaneurysms, best seen on FA (Fig. 14.122).
   - Macular oedema, hard exudates and flame-shaped retinal haemorrhages (Fig. 14.123).
   - Papillopathy, widespread arteriolar occlusion and cotton wool spots.
   - Proliferative retinopathy and tractional retinal detachment.
3. **Treatment** by laser photocoagulation may be beneficial for macular oedema and proliferative retinopathy. Papillopathy is treated with systemic steroids.
4. **Prognosis** depends on the severity of involvement. Poor prognostic features include papillopathy and proliferative retinopathy, which may result in vitreous haemorrhage and tractional retinal detachment.

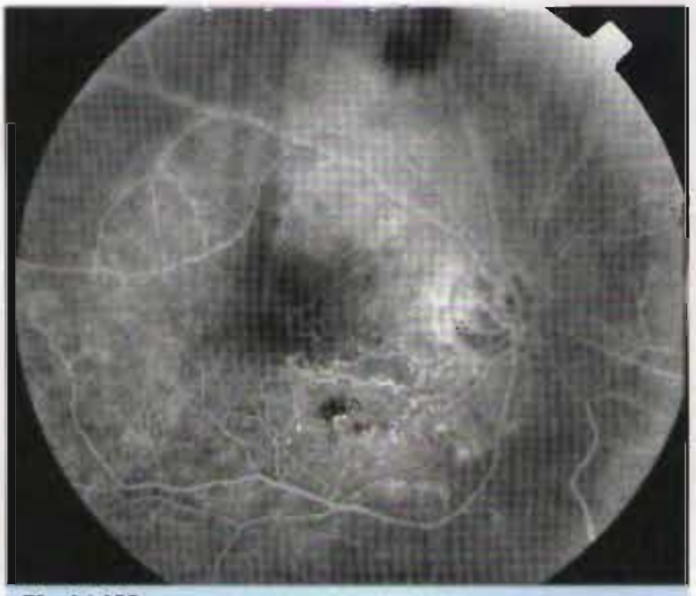


Fig. 14.122
FA of early radiation retinopathy showing focal retinal capillary non-perfusion associated with microvascular changes (Courtesy of S. Miłewski)

Purtscher retinopathy

Purtscher retinopathy is caused by microvascular damage with occlusion and ischaemia associated with (a) *severe head trauma*, (b) *chest compression injury*, (c) *embolism* (fat, air or amniotic fluid) and (d) *systemic diseases* (acute pancreatitis, pancreatic carcinoma, connective tissue diseases, lymphomas, thrombotic thrombocytopenic purpura and following bone marrow transplantation).

1. **Signs**. Multiple, superficial, white retinal patches, resembling large cotton wool spots, often associated with superficial peripapillary haemorrhages (Fig. 14.124).
2. **FA** shows variable capillary non-perfusion and blockage of background choroidal fluorescence by haemorrhages and oedema.
3. **Treatment** of the underlying cause is desirable but not always possible.
4. **Prognosis** is guarded because although the acute fundus changes usually resolve within a few weeks permanent variable visual impairment occurs in approximately 50% of cases as a result of macular or optic nerve damage.

Fig. 14.123
Severe radiation retinopathy with macular oedema and hard exudates

Fig. 14.124
Purtscher retinopathy

Retinopathy in blood dyscrasias

Anaemia

The anaemias are a group of disorders characterized by a decrease in the number of circulating red blood cells, a decrease in the amount of haemoglobin in each cell, or both. Retinal changes in the anaemias are usually innocuous and rarely of diagnostic importance.

1. **Retinopathy** is characterized by haemorrhages, which may have white centres (Roth spots), cotton wool spots and venous tortuosity (Fig. 14.125).
   - The duration and type of anaemia do not influence the occurrence of these changes, which are more common with coexistent thrombocytopenia.
   - Flame-shaped haemorrhages and cotton wool spots may occur in the absence of other haematological abnormalities.
   - Retinal venous tortuosity appears related to the severity of anaemia.
   - Roth spots represent fibrin thrombi occluding ruptured blood vessels. They may also occur in bacterial endocarditis and leukaemia.
2. **Optic neuropathy** with centrocaecal scotomas may occur in patients with pernicious anaemia. Unless treated with vitamin B_{12} supplements, permanent optic atrophy may ensue. Pernicious anaemia may also cause dementia, peripheral neuropathy and subacute combined degeneration of the spinal cord characterized by posterior and lateral column disease.

Fig. 14.125
Retinopathy in severe anaemia with Roth spots

Leukaemia

The leukaemias are a group of neoplastic disorders characterized by abnormal proliferation of white blood cells. Ocular involvement is more commonly seen in the acute than the chronic form and virtually any ocular structure may be involved. It is, however, important to distinguish the fairly rare primary leukaemic infiltration from the more common secondary changes such as those associated with anaemia, thrombocytopenia, hyperviscosity and opportunistic infections.

1. **Retinopathy** is relatively common. The findings are similar to those in anaemia with flame-shaped haemor-

Fig. 14.126
'Leopard spot fundus' in chronic leukaemia

Fig. 14.127
Pseudo-hypopyon in acute leukaemia

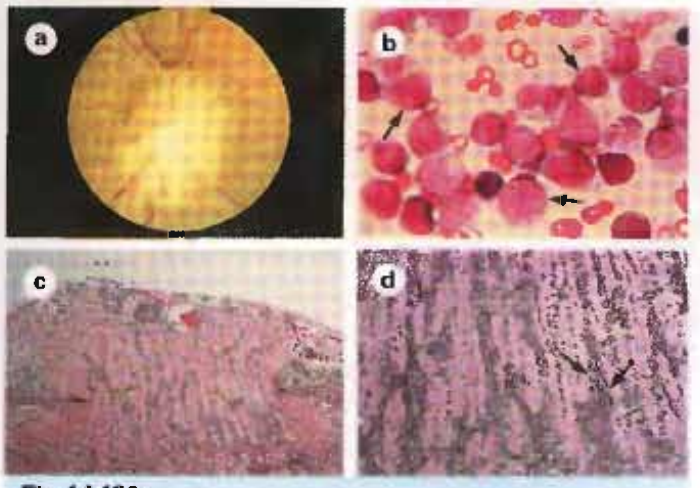


Fig. 14.128
Optic nerve infiltration in acute lymphocytic leukaemia. (a) Infiltration of the optic nerve head resulting in greyish-white elevation; (b) blood smear showing lymphoblasts; (c) disc elevation due to infiltration by leukaemic cells; (d) high-power section of retrolaminar optic nerve showing leukaemic infiltration (Courtesy of Wilmer Institute)

rhages, Roth spots and cotton wool spots. The latter may be the result of leukaemic infiltration or secondary to anaemia or hyperviscosity. Peripheral retinal neovascularization is an occasional feature of chronic myeloid leukaemia. Rarely, leukaemic pigment epitheliopathy, characterized by a 'leopard spot' fundus, may occur secondary to choroidal infiltration (Fig. 14.126).

2. Other ocular features

- Orbital involvement, particularly in children (see Fig. 17.79).

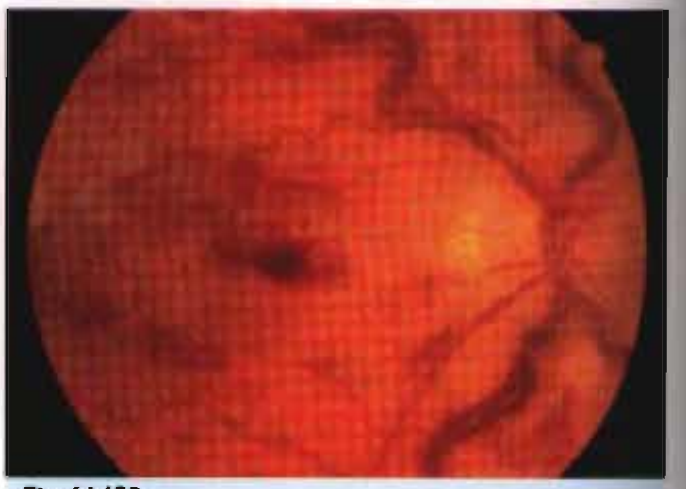


Fig. 14.129
Gross venous dilatation and haemorrhages in hyperviscosity

- Iris thickening, iritis and pseudo-hypopyon (Fig. 14.127).
- Spontaneous subconjunctival haemorrhage and hyphaema.
- Optic neuropathy due to infiltration of the optic nerve (Fig. 14.128).

Hyperviscosity states

The hyperviscosity states are a diverse group of rare disorders characterized by increased blood viscosity due to polycythaemia or abnormal plasma proteins as in Waldenström macroglobulinaemia and myeloma. Retinopathy is characterized by venous dilatation, segmentation and tortuosity, and retinal haemorrhages (Fig. 14.129).

CHAPTER 15

Hereditary Fundus Dystrophies

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Special investigations

Electroretinography

General principles

The electroretinogram (ERG) is the record of an action potential produced by the retina when it is stimulated by light of adequate intensity. The recording is made between an active electrode embedded in a contact lens placed on the patient's cornea (or a gold foil electrode placed on the eyelid) and a reference electrode on the patient's forehead. The potential between the two electrodes is then amplified and displayed (Fig. 15.1). The ERG is elicited both in the light-adapted (photopic) and dark-adapted (scotopic) states. The normal ERG is biphasic (Fig. 15.2).

1. **The a-wave** is an initial negative deflection which arises from the photoreceptors.
2. **The b-wave** is a positive deflection, which although generated by Müller cells, represents electrical activity in the bipolar cell region. The amplitude of the b-wave is measured from the trough of the a-wave to the peak of the b-wave, and increases with both dark adaptation and increased light stimulus. The b-wave consists of b1 and b2 subcomponents. The former probably represents both rod and cone activity and the latter mainly cone activity. It is possible to single out rod and cone responses with special techniques.

Normal ERG

This consists of five recordings (Fig. 15.3). The first three are elicited after 30 minutes of dark adaptation (scotopic), and the last two after 10 minutes of adaptation to moderately bright diffuse illumination (photopic).

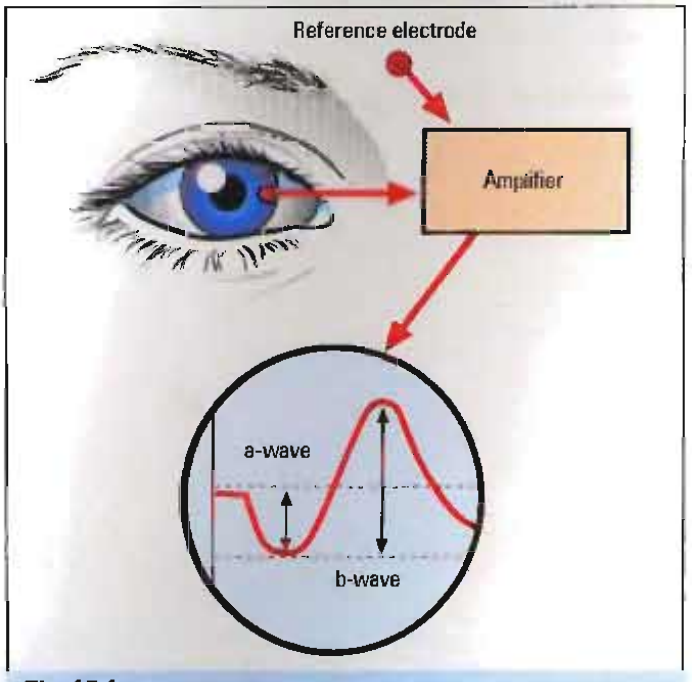


Fig. 15.1
Principles of electroretinography

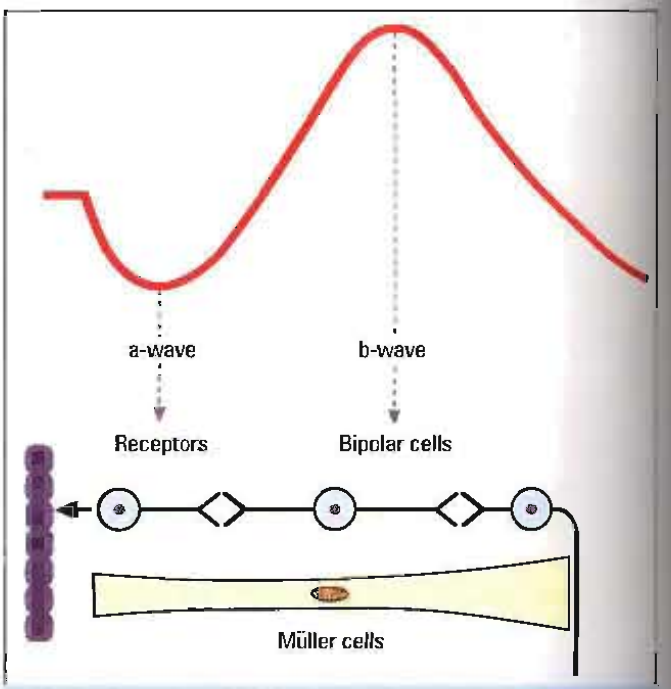


Fig. 15.2
Components and origins of the electroretinogram

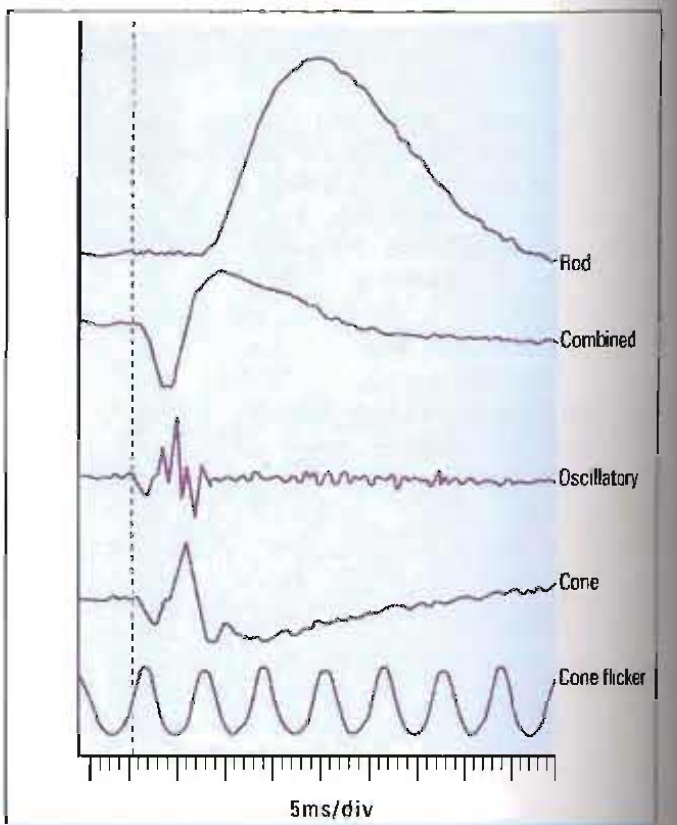


Fig. 15.3
Normal electroretinographic recordings

1. **Scotopic ERG**
   a. ***Rod*** responses are elicited with a very dim flash of white light or a blue light, resulting in a large b-wave and a small or non-recordable a-wave.
   b. ***Combined*** rod and cone responses are elicited with a very bright white flash resulting in a prominent a-wave and a b-wave.
   c. ***Oscillatory potentials*** are elicited by using a bright flash and changing the recording parameters. The oscillatory wavelets occur on the ascending limb of the b-wave and are generated by cells in the inner retina.
2. **Photopic ERG**
   a. ***Cone responses*** are elicited with a single bright flash resulting in an a-wave and a b-wave with small oscillations.
   b. ***Cone flicker*** is used to isolate cones by using a flickering light stimulus at a frequency of 30 Hz to which rods cannot respond. It provides a measure of the amplitude and implicit time of the cone b-wave. Cone responses can be elicited in normal eyes up to 50 Hz, after which point individual responses are no longer recordable (critical flicker fusion).

Electro-oculography

The electro-oculogram (EOG) measures the standing potential between the electrically positive cornea and the electrically negative back of the eye (Fig. 15.4). It reflects the activity of the RPE and the photoreceptors. This means that an eye blinded by lesions proximal to the photoreceptors will have a normal EOG. In general, diffuse or widespread disease of the RPE is needed to affect the EOG response significantly. The test is performed in both light- and dark-adapted states as follows:

1. The electrodes are attached to the skin near the medial and lateral canthi.
2. The patient is asked to look rhythmically from side to side, making excursions of constant amplitude. Each time the eye moves the cornea makes the nearest electrode positive with respect to the other.
3. The potential difference between the two electrodes is amplified and recorded.

As there is much variation in EOG amplitude in normal subjects, the result is calculated by dividing the maximal height of the potential in the light (light peak) by the minimal height of the potential in the dark (dark trough). This is expressed as a ratio (Arden ratio) or as a percentage. The normal value is over 1.85 or 185%.

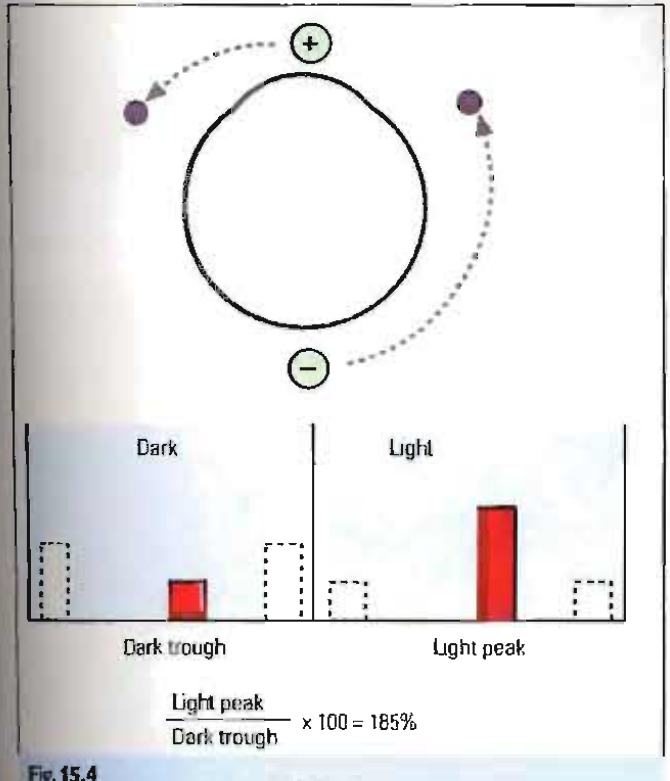


Fig. 15.4
Principles of electro-oculography

Dark adaptometry

Dark adaptation (DA) is the phenomenon by which the visual system (pupil, retina and occipital cortex) adapts to decreased illumination. Dark adaptometry is particularly useful in patients complaining of night-blindness (nyctalopia).

1. **Goldmann–Weekes** adaptometry is performed as follows:
   a. The subject is first exposed to an intense light that will totally bleach the photoreceptors.
   b. After so being rendered fully light-adapted, the subject is then suddenly placed in scotopic conditions.
   c. A series of flashes of light of gradually increasing intensity, localized 11° below fixation, is then presented.
   d. The threshold at which the subject just perceives the light is plotted.
   e. The flashes are repeated at regular intervals: the sensitivity of the eye to light gradually increases.
2. **The sensitivity curve** is bipartite (Fig. 15.5).
   - The initial rapid segment represents cone function and the second, slower segment rod function.

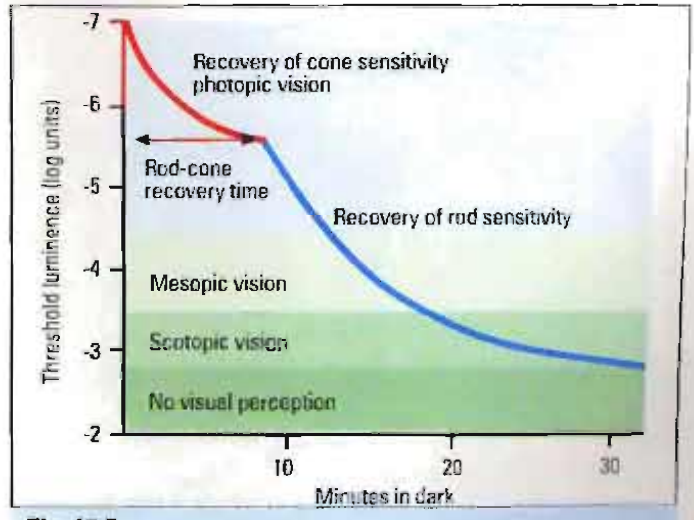


Fig. 15.5
Dark adaptation curve

- The inflection on the curve where rod adaptation begins is called the rod–cone break (alpha point) and in the normal subject occurs 7–10 minutes after exposure to a scotopic environment.
- If the flashes are focused onto the foveola (where rods are absent), only a rapid segment, corresponding to cone adaptation is recorded.

Colour vision

Assessment of colour vision (CV) is sometimes useful in the clinical evaluation of hereditary fundus dystrophies, where impairment may be present prior to the development of visual acuity and visual field changes.

General principles

CV is a function of three populations of retinal cones each with its specific sensitivity: blue (tritan) at 414–424 nm, green (deuteran) 522–539 nm and red (protan) at 549–570 nm. A normal person requires all these primary colours to match those within the spectrum. Any given cone pigment may be deficient (e.g. protanomaly: red weakness) or entirely absent (e.g. protanopia: red blindness). Trichromats possess all three types of cones (although not necessarily functioning perfectly) while absence of one or two types of cones renders an individual a dichromat or a monochromat respectively. Most individuals with congenital colour defects are anomalous trichromats and use abnormal proportions of the three primary colours to match those in the light spectrum. Those with red–green deficiency caused by abnormality of red-sensitive cones are protanomalous, those with abnormality of green-sensitive cones are deuteranomalous and those with blue–green deficiency caused by abnormality of blue-sensitive cones are tritanomalous.

> *NB:* Acquired macular disease tends to produce blue–yellow defects and optic nerve lesions red–green defects.

Colour vision tests

1. **Ishihara** test is used mainly to screen for congenital protan and deuteran defects. It consists of a test plate followed by 16 plates each with a matrix of dots arranged to show a central shape or number which the subject is asked to identify (Fig. 15.6). A colour-deficient person will only be able to identify some of the figures. Inability to identify the test plate (provided visual acuity is sufficient) indicates malingering.
2. **City University** consists of 10 plates each containing a central colour and four peripheral colours (Fig. 15.7). The subject selects the peripheral colour which most closely matches the central colour.
3. **Hardy–Rand–Rittler** is similar to Ishihara but more sensitive since it can detect all three congenital defects.
4. **Farnsworth–Munsell 100-hue** is the most sensitive for both congenital and acquired colour defects but is seldom used in practice. Despite the name it consists of 85 hue caps contained in four separate racks in each of which the two end caps are fixed while the others are loose, so they can be randomized by the examiner (Fig. 15.8).
   a. The subject is asked to rearrange the loose randomized caps 'in their natural' order in one box.
   b. The box is then closed, turned upside down and then opened so that the markers on the inside of the caps become visible.

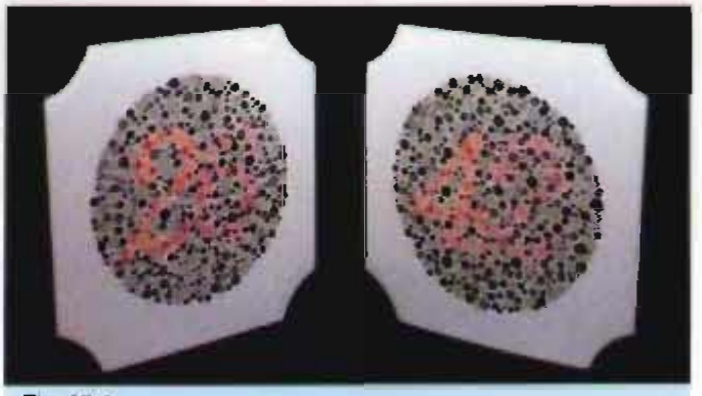


Fig. 15.6
Ishihara pseudo-isochromatic plates

Fig. 15.7
City University test

Fig. 15.8
Farnsworth–Munsell 100-hue test

c. The findings are then recorded in a simple cumulative manner on a circular chart.
d. Each of the three forms of dichromatism is characterized by failure in a specific meridian of the chart.

5. **Farnsworth D15** hue discrimination test is similar to the Farnsworth–Munsell 100-hue test but utilizes only 15 caps.

Retinal dystrophies

Retinitis pigmentosa

Retinitis pigmentosa (RP), perhaps better termed pigmentary retinal dystrophy, due to the absence of inflammation, is a diffuse retinal dystrophy predominantly affecting the rod system. Its prevalence is 1:5000.

Inheritance

The age of onset, rate of progression, eventual visual loss and associated ocular features are frequently related to the mode of inheritance. Many cases are due to mutation of the rhodopsin gene. RP may occur as an isolated sporadic disorder, or be inherited in an autosomal dominant (AD), autosomal recessive (AR) or X-linked (XL) manner. It may also be associated with certain systemic disorders which are usually AR.

1. **Isolated**, without any family history, is common.
2. **AD** is also common and has the best prognosis.
3. **AR** is less common and has an intermediate prognosis.
4. **XL** is the least common but most severe. Female carriers may have normal fundi or exhibit a golden-metallic tapetal reflex temporal to the macula and atrophic and pigmentary peripheral irregularities.

Clinical features

Diagnostic criteria for RP are bilateral involvement, loss of peripheral vision and progressive loss of predominantly rod photoreceptor function. The classic clinical triad of RP is (a) *arteriolar attenuation*, (b) *retinal bone-spicule pigmentation* and (c) *waxy disc pallor*.

1. **Presentation** is with nyctalopia during the third decade but may be sooner depending on the pedigree.
2. **Signs** (in chronological order)
   - Arteriolar narrowing, fine dust-like intraretinal pigmentation and loss of RPE, an appearance previously referred to as RP *sine pigmento* (Fig. 15.9). A minority of patients have scattered white dots, most numerous at the equator; this is referred to as *retinitis punctata albescens* (Fig. 15.10).
   - Mid-peripheral, coarse, perivascular 'bone-spicule' pigmentary changes (Fig. 15.11).
   - Gradual increase in density of the pigmentary changes with spread anteriorly and posteriorly (Fig. 15.12).

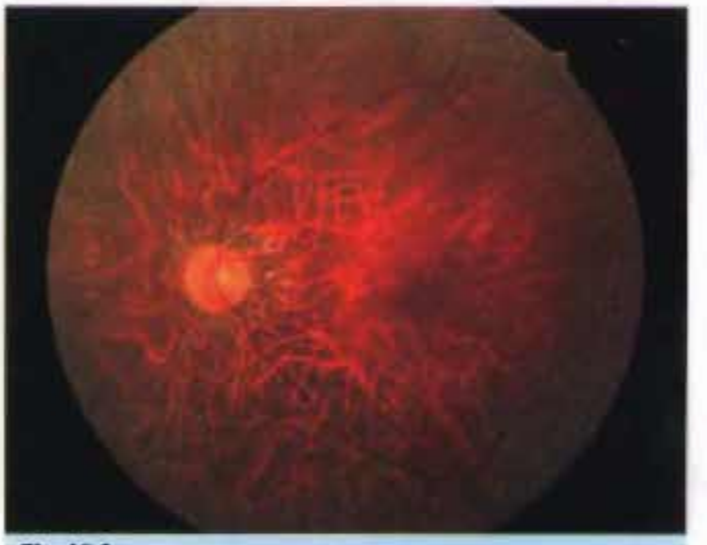


Fig. 15.9
Retinitis pigmentosa with vascular attenuation and minimal pigmentary changes

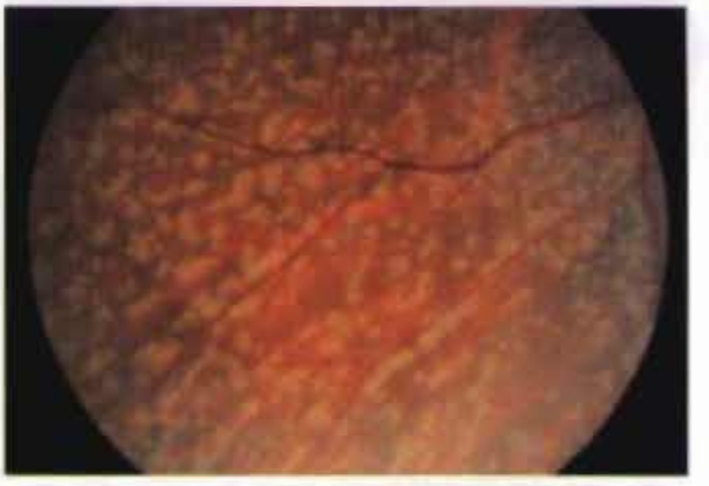


Fig. 15.10
Retinitis punctata albescens

   - Tessellated fundus appearance, due to RPE atrophy and unmasking of large choroidal vessels, severe arteriolar attenuation and waxy disc pallor (Fig. 15.13).

Fig. 15.11
'Bone spicule' pigmentary changes in retinitis pigmentosa

Fig. 15.12
Advanced retinitis pigmentosa

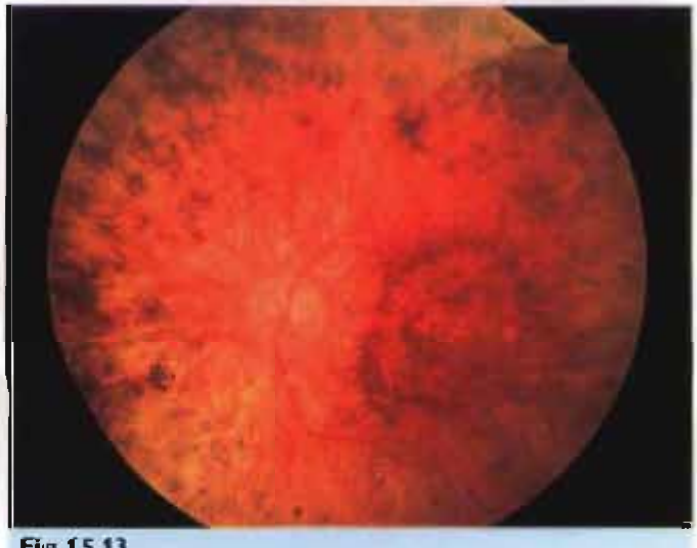


Fig. 15.13
Advanced retinitis pigmentosa with unmasking of choroidal vessels

3. **Maculopathy** may be atrophic, cellophane or CMO: the latter may respond to systemic acetazolamide.

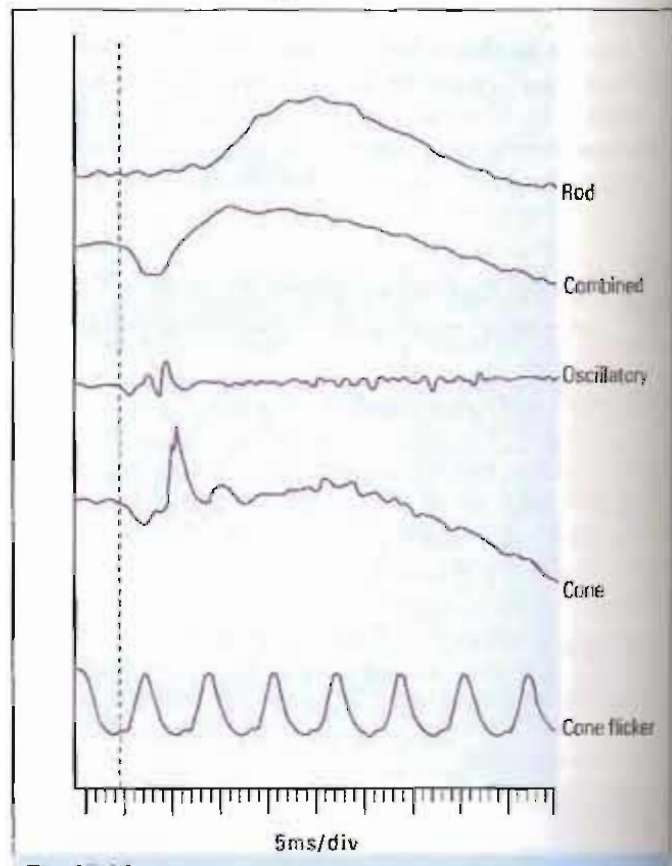


Fig. 15.14
Electroretinogram in retinitis pigmentosa (see text)

4. **ERG** initially shows reduced scotopic rod and combined responses (Fig. 15.14); later photopic responses become reduced.
5. **EOG** is subnormal.
6. **DA** is prolonged and may be useful in early cases where the diagnosis is uncertain.
7. **CV** is normal.
8. **Perimetry** classically demonstrates an annular mid-peripheral scotoma, which expands both peripherally and centrally. It ultimately leaves a tiny island of central vision which may eventually be extinguished.
9. **FA**, not required to make the diagnosis, shows diffuse hyperfluorescence due to window defects and small areas of hypofluorescence corresponding to masking by pigment (Fig. 15.15b).

Prognosis

The long-term prognosis is poor, with eventual loss of central vision due to direct involvement of the fovea by RP itself or maculopathy. Daily administration of supplemental vitamin A, if instituted early, may retard the progression of RP. The overall prognosis is as follows:

- About 25% of patients maintain good visual acuity and are able to read throughout their working lives, despite unrecordable ERG and 2–3° central field.
- Under the age of 20 years, most patients have a visual acuity better than 6/60.

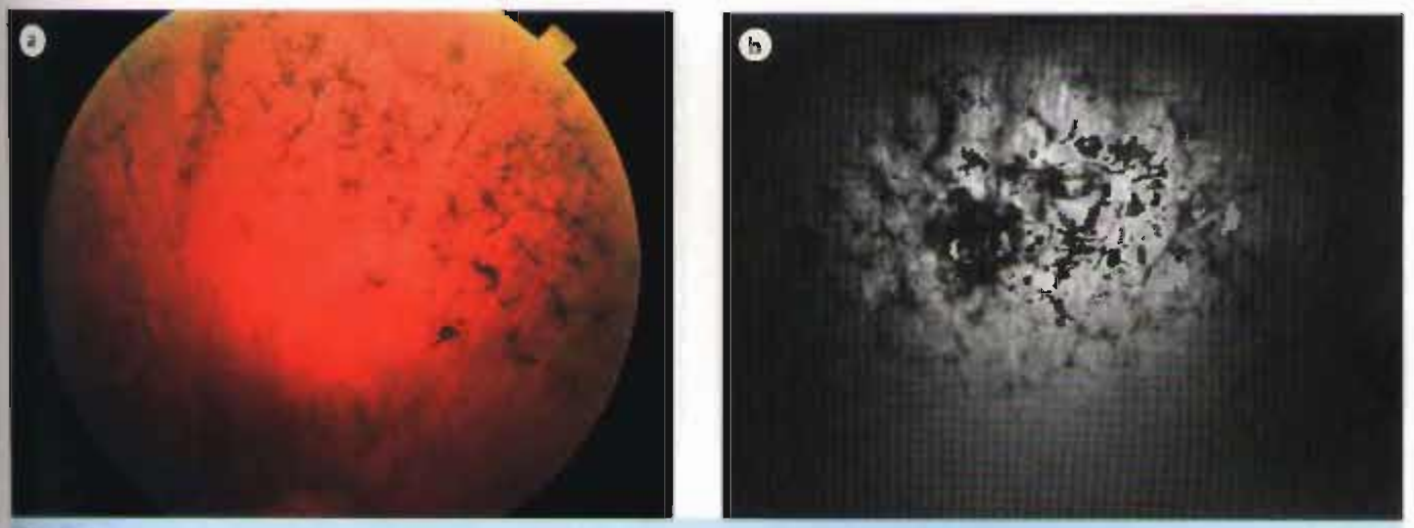


Fig. 15.15
(a) Retinitis pigmentosa; (b) FA showing diffuse hyperfluorescence due to window defects and focal hypofluorescence due to masking by pigment

- By the age of 50 years an appreciable number have a visual acuity of worse than 6/60.

Ocular associations

Regular follow-up of patients with RP is essential to detect other vision-threatening complications, some of which may be amenable to treatment.

1. **Posterior subcapsular cataracts** are common in all forms of RP; surgery is often beneficial.
2. **Open-angle glaucoma** occurs in 3% of patients.
3. **Myopia** is frequent.
4. **Keratoconus** is uncommon.
5. **Vitreous changes**, which are common, consist of posterior vitreous detachment and occasionally intermediate uveitis.
6. **Optic disc drusen** are more frequently seen than in normals (Fig. 15.16).

Atypical RP

1. **Sector RP** is characterized by involvement of one quadrant (usually nasal) (Fig. 15.17) or one half (usually inferior). Progression is slow and many cases remain stationary.
2. **Pericentral RP** in which the pigmentary abnormalities emanate from the disc and extend along the temporal arcades and nasally.
3. **RP with exudative vasculopathy** is characterized by a Coats-like appearance with lipid deposition in the peripheral retina and exudative retinal detachment.

Differential diagnosis

1. **End-stage chloroquine retinopathy**
   - Similarities: bilateral diffuse loss of RPE with unmasking of choroidal vessels and arteriolar attenuation.

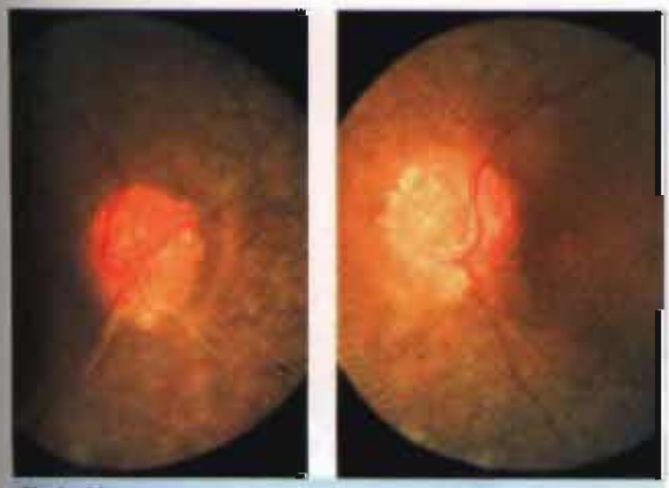


Fig. 15.16
Optic disc drusen associated with retinitis pigmentosa

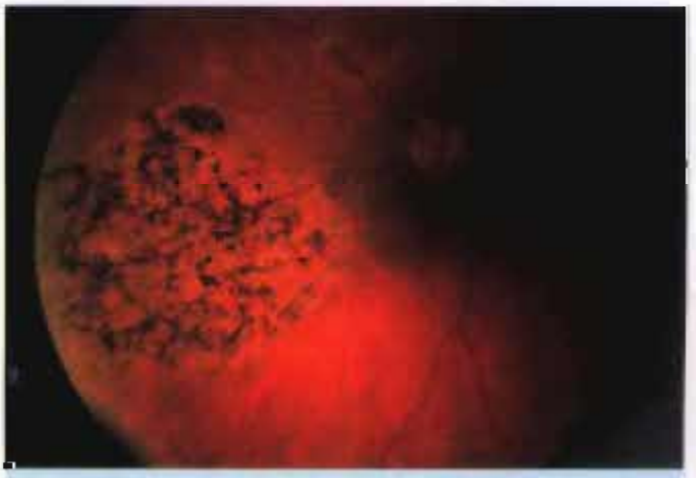


Fig. 15.17
Sector retinitis pigmentosa

- Differences: pigmentary changes do not have a perivascular 'bone corpuscle' configuration; optic atrophy is not waxy.

2. **End-stage thioridazine retinopathy**
   - Similarities: bilateral diffuse loss of RPE.
   - Differences: plaque-like pigmentary changes and absence of nyctalopia.
3. **End-stage syphilitic neuroretinitis**
   - Similarities: gross restriction of visual fields, vascular attenuation and pigmentary changes.
   - Differences: nyctalopia is mild, asymmetrical involvement with mild or absent choroidal unmasking.
4. **Cancer-related retinopathy**
   - Similarities: nyctalopia, restriction of peripheral visual field, arteriolar attenuation and extinguished ERG.
   - Differences: more rapid course and mild or absent pigmentary changes.

Fig. 15.18
Central retinitis pigmentosa in Kearns–Sayre syndrome

Systemic associations

RP, often atypical, may be associated with a wide variety of systemic disorders. The more important associations are described hereunder.

1. **Bassen–Kornzweig syndrome** is an AD disease due to deficiency in beta-lipoprotein resulting in intestinal malabsorption.
   a. ***Signs.*** Spinocerebellar ataxia and acanthocytosis in peripheral blood.
   b. ***Retinopathy*** develops towards the end of the first decade; the pigment clumps are often larger than in classic RP and are not confined to the equatorial region. Peripheral white dots are also common.
   c. ***Other features*** are ophthalmoplegia and ptosis.
   d. ***Treatment*** with vitamin E, if instituted early, may be beneficial for neurological disability.
2. **Refsum disease** is an AR inborn error of metabolism due to a deficiency in the enzyme phytanic acid 2-hydroxylase resulting in the accumulation of phytanic acid in the blood and body tissues.
   a. ***Signs*** include polyneuropathy, cerebellar ataxia, deafness, anosmia, cardiomyopathy, ichthyosis and elevated CSF protein in the absence of pleocytosis (cytoalbuminous inversion).
   b. ***Retinopathy*** develops in the second decade and is characterized by generalized 'salt-and-pepper' changes.
   c. ***Other features*** include cataract, miosis and prominent corneal nerves.
   d. ***Treatment***, initially with plasmapheresis and later with a phytanic-acid-free diet, may prevent progression of both systemic and retinal involvement.
3. **Usher syndrome** is a distressing AR condition which accounts for about 5% of all cases of profound deafness in children, and is responsible for about half of all cases of combined deafness and blindness. RP develops before puberty.
4. **Kearns–Sayre syndrome** is a mitochondrial cytopathy associated with mitochondrial DNA deletions (see Chapter 20). Atypical RP is characterized by coarse pigment clumping which principally affects the central fundus (Fig. 15.18).
5. **Bardet–Biedl syndrome** is characterized by mental handicap, polydactyly, obesity and hypogenitalism. RP is serious and almost 75% of patients are blind by the age of 20 years. Some patients develop a bull's eye maculopathy.

Progressive cone dystrophy

Progressive cone dystrophies comprise a heterogeneous group of rare disorders. Patients with pure cone dystrophy initially have only cone dysfunction. Those with cone–rod dystrophy have an associated but less severe rod dysfunction. However, in many patients with initially pure cone dysfunction the rod system becomes subsequently affected. The term 'cone–rod dystrophy' is therefore more appropriate.

1. **Inheritance.** Most cases are sporadic; of the remainder the most frequent established inheritance pattern is AD but the condition may also be AR or XL.
2. **Presentation** is in the first to third decades with gradual bilateral impairment of central and colour vision which may later be associated with photophobia and pendular nystagmus.
3. **Signs** (in chronological order)
   - The fovea may be normal or exhibit non-specific granularity.
   - Bull's eye maculopathy (Fig. 15.19) is classically described but not universal.
   - Mid-peripheral 'bone-spicule' pigmentation, arteriolar attenuation and temporal disc pallor may develop (Fig. 15.20).

Fig. 15.19
Cone dystrophy with 'bull's eye' maculopathy

Fig. 15.20
Cone dystrophy with mild 'bone-spicule' pigmentary changes

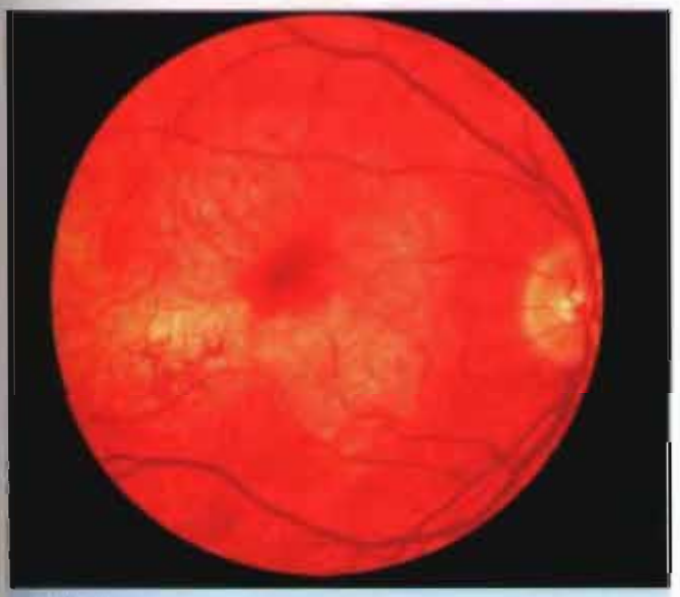


Fig. 15.21
Advanced cone dystrophy with atrophic maculopathy

- Progressive RPE atrophy at the macula with eventual geographic atrophy (Fig. 15.21).

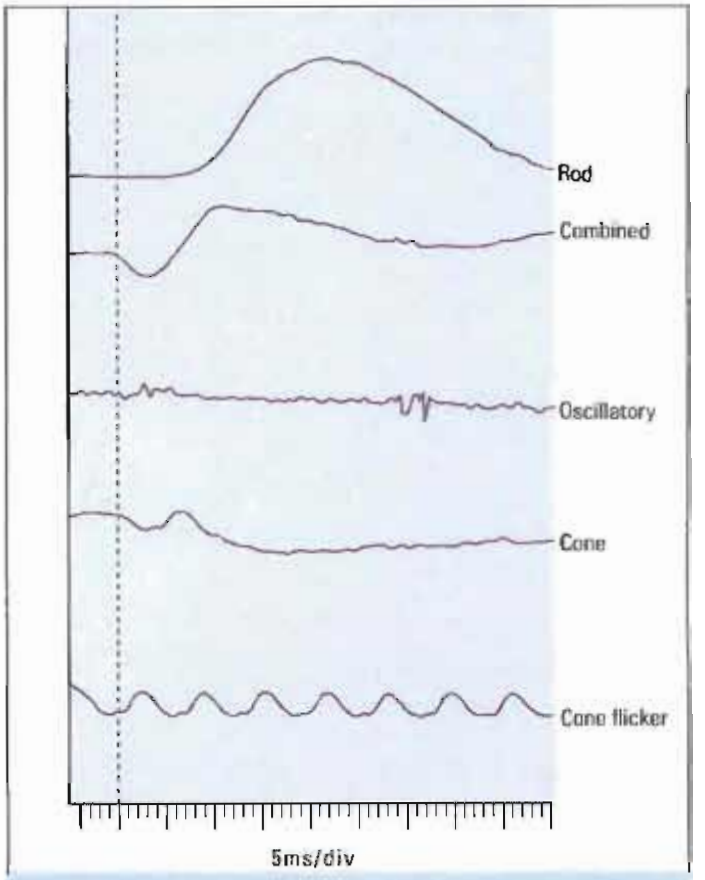


Fig. 15.22
Electroretinogram in cone dystrophy (see *text*)

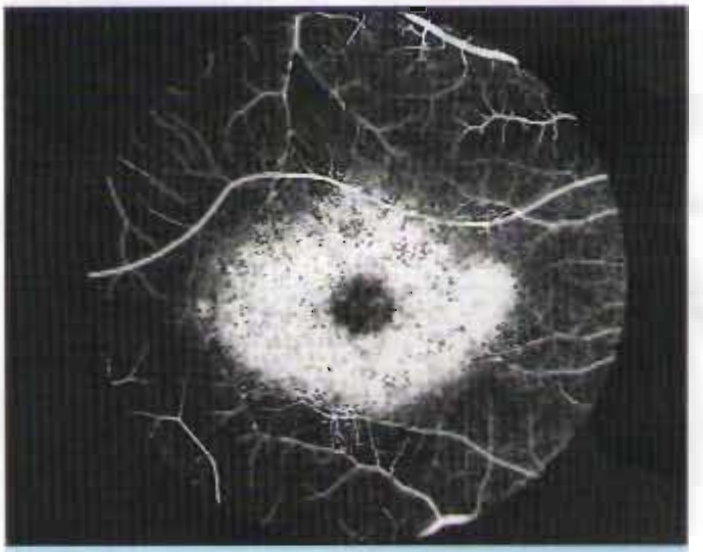


Fig. 15.23
FA in cone dystrophy showing a 'bull's eye' pattern due to a window defect

4. **ERG**. Photopic is abnormal or non-recordable; flicker fusion frequency is reduced; rod responses are preserved until late (Fig. 15.22).
5. **EOG** is normal to subnormal.
6. **DA**. Cone segment is abnormal; rod segment is initially normal but may become subnormal later.
7. **CV** shows a severe deuteran–tritan defect out of proportion to visual acuity.

8. **FA** of bull's eye maculopathy shows a round hyperfluorescent window defect with a hypofluorescent centre (Fig. 15.23).
9. **Prognosis** depends on the severity of rod involvement; minimal involvement has a better prognosis, at least in the intermediate term.
10. **Differential diagnosis** of bull's eye macula includes chloroquine maculopathy, advanced Stargardt disease, fenestrated sheen dystrophy, benign concentric annular macular dystrophy and Batten disease.

Stargardt disease

Stargardt disease (juvenile macular dystrophy) and fundus flavimaculatus are regarded as variants of the same disease despite presenting at different times and carrying different prognoses.

1. **Inheritance** is AR with the gene locus ABC4R on 1p21–22.
2. **Presentation** is in the first to second decades with bilateral, gradual impairment of central vision which may be out of proportion to the macular changes, so that the child may be suspected of malingering.
3. **Signs** (in chronological order)
   - The fovea may be normal or show non-specific mottling (Fig. 15.24).
   - Oval, 'snail-slime' or 'beaten-bronze' foveal appearance, which may be surrounded by yellow-white flecks (Fig. 15.25).
   - Geographic atrophy which may have bull's eye configuration (Fig. 15.26).
4. **ERG**. Photopic is normal to subnormal; scotopic is normal.
5. **EOG** is subnormal in advanced cases.
6. **CV** shows deuteran–tritan defects.

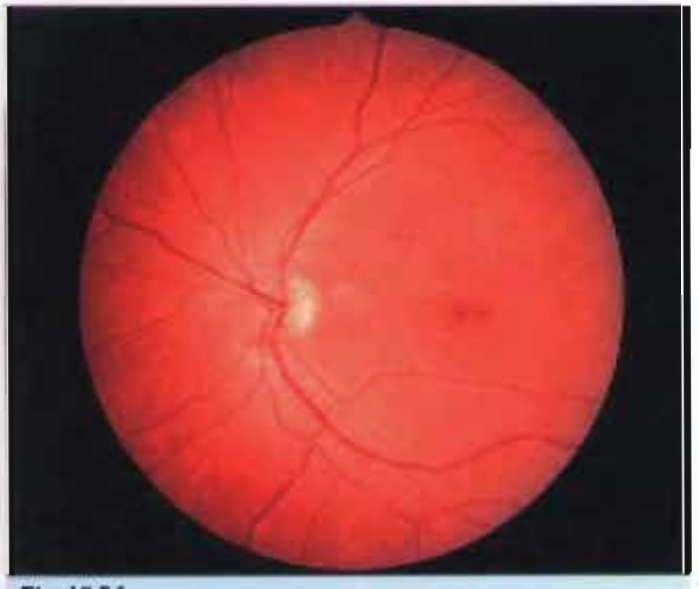


Fig. 15.24
Early Stargardt macular dystrophy

Fig. 15.25
Stargardt macular dystrophy with surrounding flecks

Fig. 15.26
Advanced Stargardt macular dystrophy

7. **FA** often shows a 'dark choroid' due to lipofuscin deposit within the RPE. It is characterized by absence of normal background fluorescence, which enhances the prominence of the retinal circulation. Eyes with geographic atrophy show a window defect at the macula (Fig. 15.27).
8. **Prognosis** is poor; once visual acuity drops below 6/12 it tends to decrease rapidly and stabilize at about 6/60.

Fundus flavimaculatus

1. **Inheritance** is AR.
2. **Presentation** is in adult life, although in the absence of macular involvement the condition may be asymptomatic and discovered by chance.
3. **Signs** (in chronological order)
   - Bilateral, ill-defined, yellow-white flecks, at the level of the RPE, scattered throughout the posterior pole and

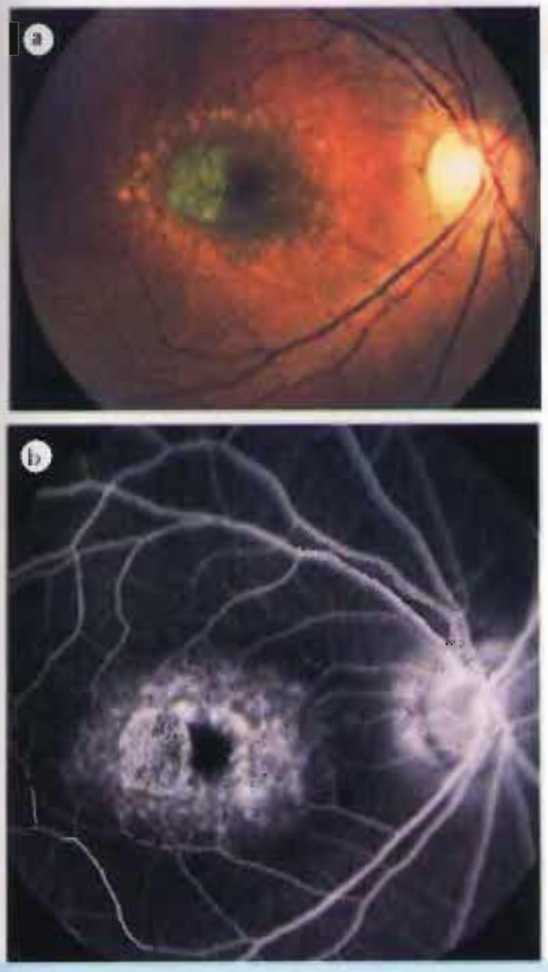


Fig. 15.27
(a) Stargardt macular dystrophy; (b) FA showing macular hyperfluorescence due to a window defect and a dark choroid (Courtesy of S. Milewski)

mid-periphery. The flecks may be round, oval, linear, semilunar or pisciform (fish-tail-like) (Fig. 15.28).
- The fundus has a vermilion colour in about 50% of cases.
- New lesions develop as older ones become ill-defined and softer (*see* Fig. 15.30a).
- Geographic atrophy develops in some cases (Fig. 15.29).

4. **ERG**. Photopic is normal to subnormal: scotopic is normal.
5. **EOG** is subnormal.
6. **CV** is normal.
7. **FA** shows a generalized 'dark choroid'. Fresh flecks show early blockage and late staining; old flecks show RPE window defects (Fig. 15.30b).
8. **Prognosis** is relatively good and patients may remain asymptomatic for many years unless one of the flecks involves the foveola or geographic atrophy develops.
9. **Differential diagnosis** of retinal flecks includes dominant drusen, fundus albipunctatus, early North Carolina macular dystrophy and benign fleck retina syndrome.

Juvenile Best disease

Juvenile Best disease (vitelliform dystrophy) is a rare condition which evolves gradually through five stages.

1. **Inheritance** is AD with variable penetrance and expressivity with the gene locus on 11q13.
2. **Stage 0** (pre-vitelliform) is characterized by a subnormal EOG in an asymptomatic child with a normal fundus appearance.
3. **Stage I** is characterized by pigment mottling at the macula.

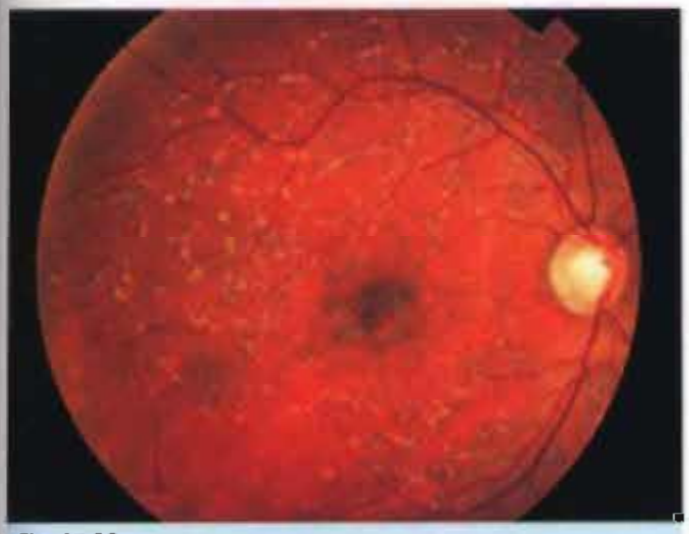


Fig. 15.28
Fundus flavimaculatus (Courtesy of S. Milewski)

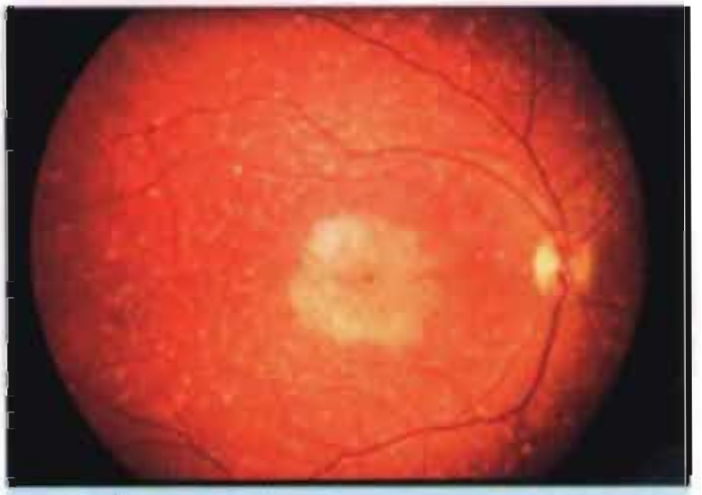


Fig. 15.29
Fundus flavimaculatus with atrophic maculopathy (Courtesy of S. Milewski)

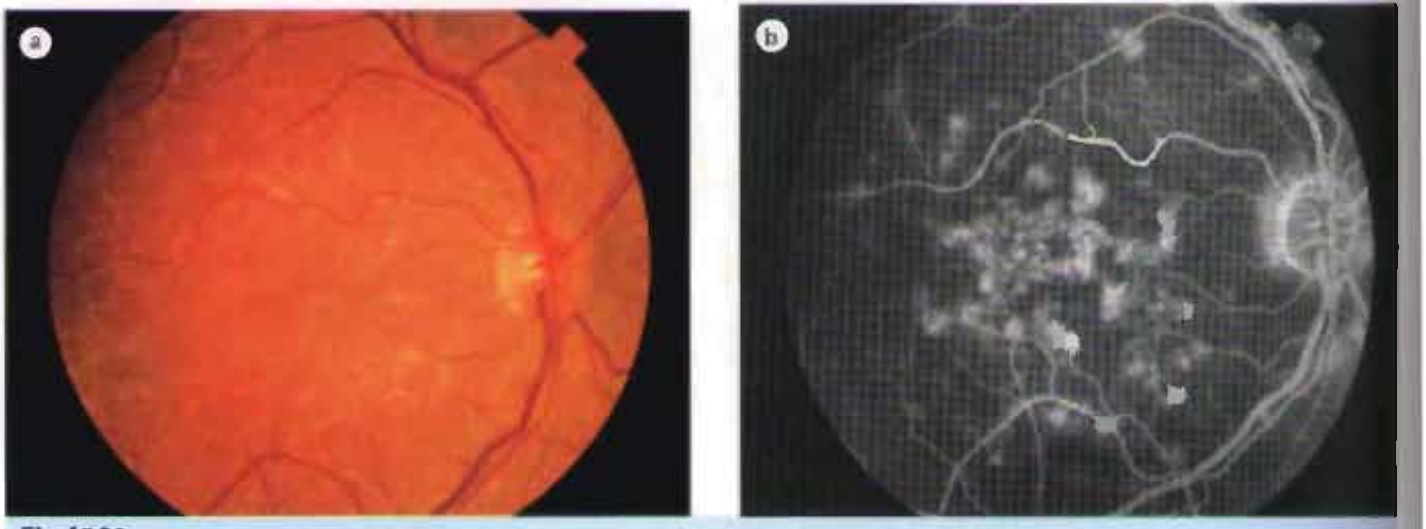


Fig. 15.30
(a) Advanced fundus flavimaculatus; (b) FA showing hyperfluorescence of the flecks and a dark choroid (Courtesy of S. Milewski)

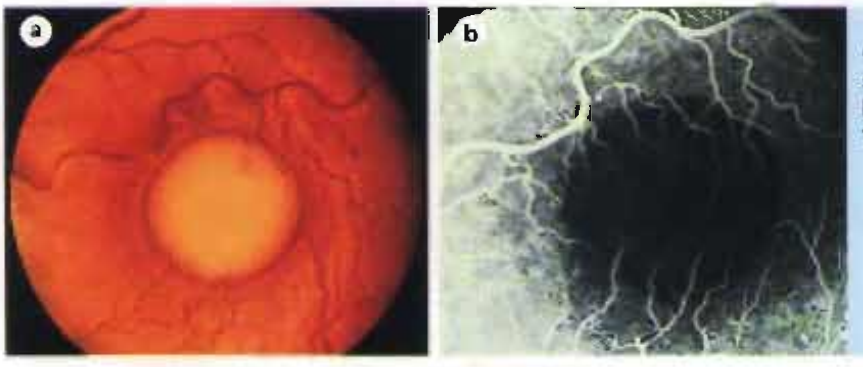


Fig. 15.31
(a) Vitelliform stage of juvenile Best disease; (b) FA showing hypofluorescence due to blocked background choroidal fluorescence (Courtesy of Wilmer Institute)

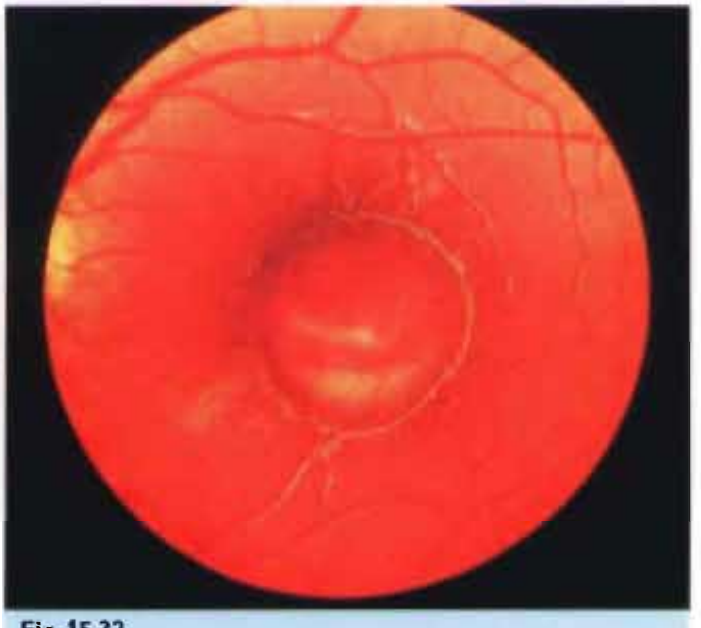


Fig. 15.32
Pseudo-hypopyon stage of juvenile Best disease (Courtesy of P. Morse)

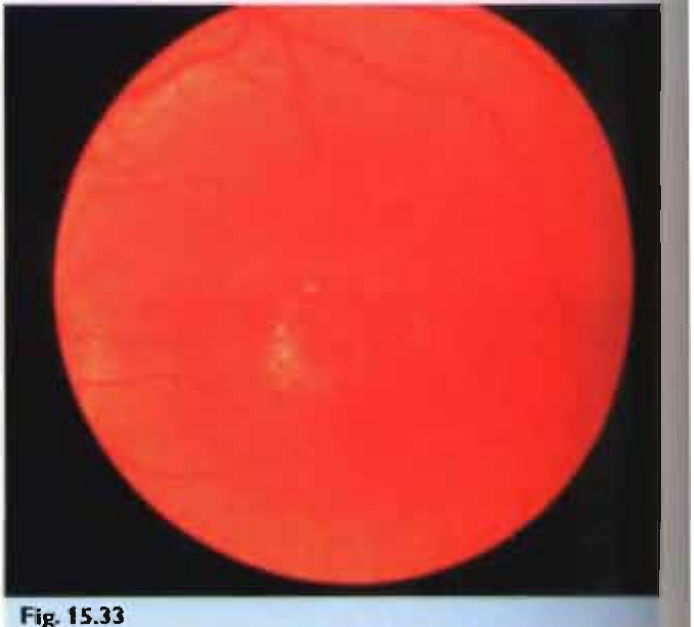


Fig. 15.33
Vitelliruptive stage of juvenile Best disease (Courtesy of P. Morse)

4. **Stage 2** (vitelliform), which develops in the first to second decades, is characterized by a round egg-yolk ('sunny side up') macular lesion consisting of subretinal lipofuscin (Fig. 15.31a). Visual acuity may be normal or slightly decreased.
5. **Stage 3** (pseudo-hypopyon) may occur when part of the lesion becomes absorbed (Fig. 15.32). Occasionally, the whole lesion becomes absorbed with little effect on vision.
6. **Stage 4** (vitelliruptive) in which the egg yolk begins to break up ('scrambled egg') (Fig. 15.33) and visual acuity drops.

7. **ERG** is normal.
8. **EOG** is severely subnormal during all stages and in carriers with normal fundi.
9. **CV** defects are proportional to the degree of visual loss.
10. **FA** during the vitelliform stage shows blockage of background choroidal fluorescence (*see* Fig. 15.31b).
11. **Prognosis** is reasonably good until the fifth decade, after which visual acuity declines and some patients become legally blind due to macular scarring, CNV, geographic atrophy or hole formation which may lead to retinal detachment.

Adult vitelliform foveomacular dystrophy

Adult vitelliform foveomacular dystrophy is considered as belonging to the category of 'pattern dystrophies'. In contrast to juvenile Best disease the foveal lesions are smaller, present later and do not demonstrate evolutionary changes.

1. **Inheritance** is probably AD with the gene locus on 6p21–22.
2. **Presentation** is in the fourth to sixth decades with mild metamorphopsia although often the condition is discovered by chance.
3. **Signs.** Bilateral, symmetrical, round, slightly elevated, yellow, subfoveal lesions about one-third disc diameter in size (Fig. 15.34).
4. **ERG** is normal.
5. **EOG** is normal to moderately subnormal.
6. **CV** shows a mild tritan defect.
7. **FA** shows central hypofluorescence surrounded by a small irregular hyperfluorescent ring.
8. **Prognosis** is good in the majority of cases.

Fig. 15.34
Adult vitelliform macular dystrophy

Fig. 15.35
Multifocal Best disease (Courtesy of C. Barry)

Multifocal Best disease

Multifocal Best disease is very unusual (Fig. 15.35) and may occur without a family history. It may develop acutely in adult life and give rise to diagnostic difficulties.

Familial drusen

Familial drusen (Doyne honeycomb choroiditis, malattia levantinese) is thought to represent an early manifestation of age-related macular degeneration.

1. **Inheritance** is AD with full penetrance but variable expressivity. The gene locus EFEMP1 is on 2p16.
2. **Clinical features**
   a. *Mild* disease is characterized by a few small, discrete, hard drusen confined to the macula (Fig. 15.36). The lesions typically appear in the third decade and are innocuous.

Fig. 15.36
Mild familial dominant drusen

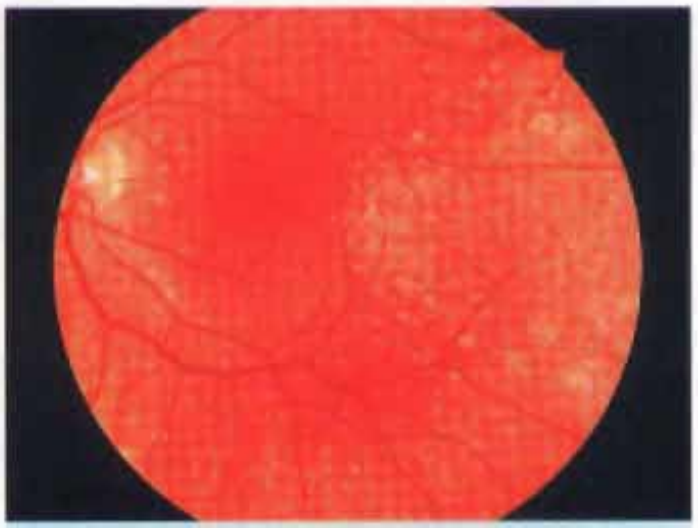


Fig. 15.37
Advanced familial dominant drusen

Fig. 15.39
FA in familial dominant drusen showing numerous well-defined hyperfluorescent spots

*b. **Moderate*** disease is characterized by large, soft drusen at the posterior pole and parapapillary region (Fig. 15.37). The lesions appear after the third decade and are associated with normal or mild impairment of visual acuity.

*c. **Advanced*** disease is uncommon and presents after the fifth decade with CNV or geographic atrophy.

*d. **Malattia leventinese*** shares phenotypic overlap with familial drusen. It is characterized by small, innumerable, basal laminar drusen with a spoke-like or radial distribution centred on the fovea and parapapillary area (Fig. 15.38). Most patients are asymptomatic until the fourth to fifth decades, when they may develop CNV or geographic atrophy.

3. **ERG** is normal.
4. **EOG** is subnormal in patients with advanced disease.
5. **FA** shows well-defined hyperfluorescent spots due to window defects which are more extensive on FA (Fig. 15.39) than on clinical examination.

Sorsby pseudo-inflammatory macular dystrophy

Sorsby pseudo-inflammatory macular dystrophy, also referred to as hereditary haemorrhagic macular dystrophy, is a very rare but serious condition.

1. **Inheritance** is AD with full penetrance; the gene TIMP3 is on 22q12.1–13.2.
2. **Presentation** is in the fifth decade with bilateral exudative maculopathy.
3. **Signs** (in chronological order)
   - Yellow-white, confluent, drusen-like deposits along the arcades, nasal to the disc and mid-periphery (Fig. 15.40).
   - CNV and exudative maculopathy (Fig. 15.41).
   - Subretinal scarring (Fig. 15.42).
4. **ERG** is initially normal but may be subnormal in late disease.

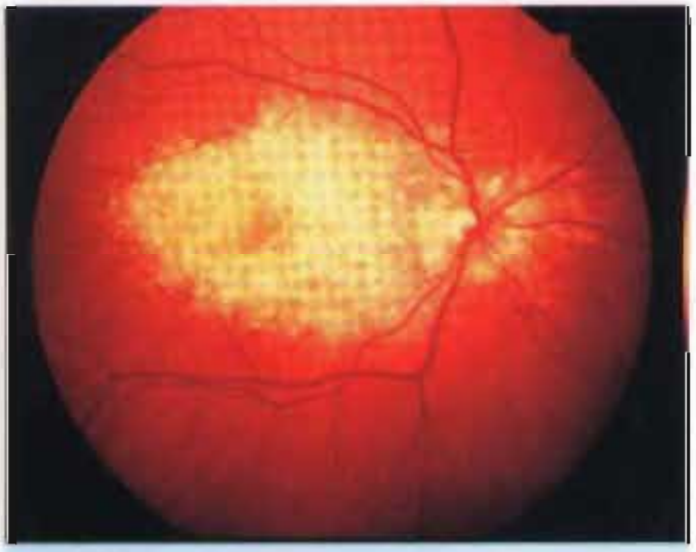


Fig. 15.38
Malattia leventinese (Courtesy of Moorfields Eye Hospital)

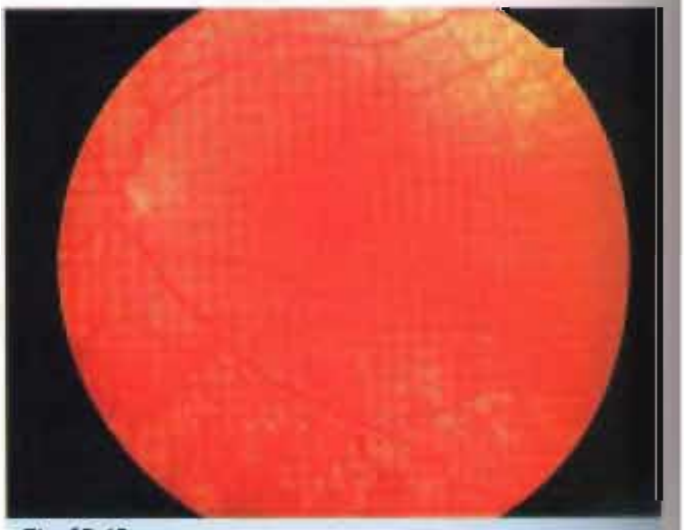


Fig. 15.40
Early Sorsby pseudo-inflammatory macular dystrophy with confluent flecks

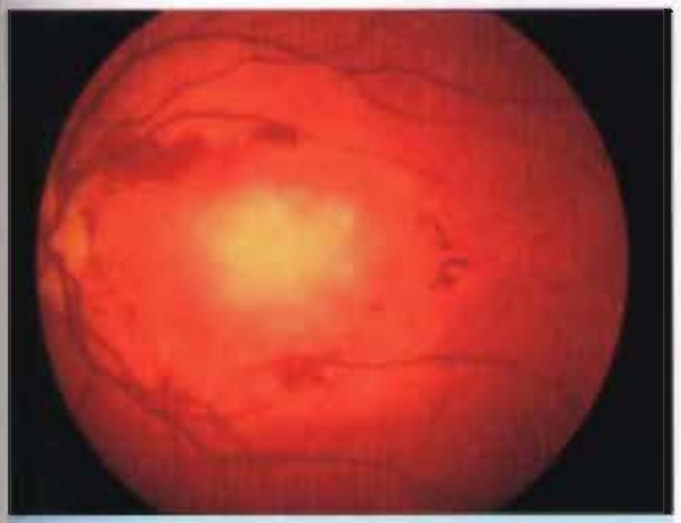


Fig. 15.41
Exudative maculopathy in Sorsby pseudo-inflammatory macular dystrophy

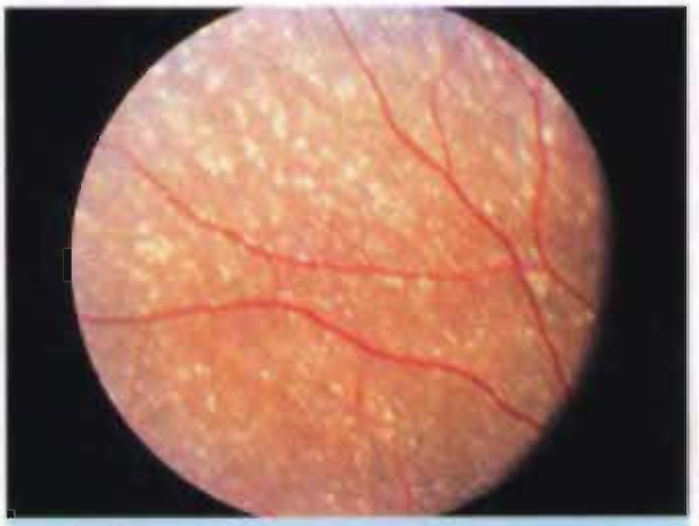


Fig. 15.43
Peripheral flecks in grade 1 North Carolina macular dystrophy (Courtesy of P. Morse)

Fig. 15.42
End-stage Sorsby pseudo-inflammatory macular dystrophy

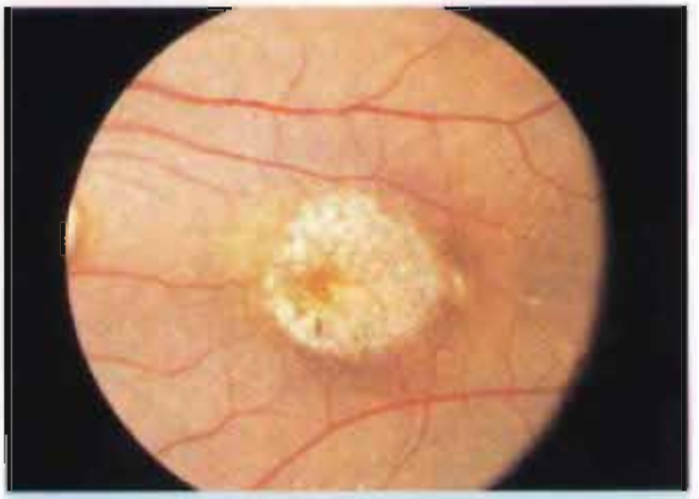


Fig. 15.44
Confluent macular flecks in grade 2 North Carolina macular dystrophy (Courtesy of P. Morse)

5. **EOG** is normal.
6. **Prognosis** is poor due to maculopathy. Some patients also lose ambulatory vision by the seventh decade due to progressive peripheral chorioretinal atrophy.

North Carolina macular dystrophy

North Carolina macular dystrophy is a very rare but serious condition.

1. **Inheritance** is AD with complete penetrance but highly variable expressivity with the gene MCDR1 on 6q.
2. **Signs and prognosis**
   a. *Grade 1* is characterized by yellow-white, drusen-like peripheral (Fig. 15.43) and macular deposits which develop during the first decade and may remain asymptomatic throughout life.
   b. *Grade 2* is characterized by deep, confluent macular deposits (Fig. 15.44). The long-term visual prognosis is less favourable because some patients develop exudative maculopathy.
   c. *Grade 3* is characterized by bilateral coloboma-like atrophic macular lesions (Fig. 15.45) with variable impairment of visual acuity.
3. **ERG** is normal.
4. **EOG** is normal.
5. **FA** in grades 1 and 2 shows transmission defects and late staining.

Butterfly macular dystrophy

Butterfly dystrophy is a rare and relatively innocuous condition.

Fig. 15.45
Coloboma-like maculopathy in grade 3 North Carolina macular dystrophy (Courtesy of Moorfields Eye Hospital)

1. **Inheritance** is probably AD.
2. **Presentation** is in the second to fifth decades usually by chance and occasionally with mild impairment of central vision.
3. **Signs**
   - Yellow pigment at the fovea arranged in a triradiate manner (Fig. 15.46).
   - Peripheral pigmentary stippling may be present.
4. **ERG** is normal.
5. **EOG** is subnormal to abnormal.
6. **FA** shows corresponding hypofluorescence.
7. **Prognosis** is excellent.

Dominant cystoid macular oedema

Dominant cystoid macular oedema is an extremely rare but serious condition.

Fig. 15.46
Butterfly dystrophy

1. **Inheritance** is AD with the gene locus on 7q.
2. **Presentation** is in the first to second decades with gradual impairment of central vision.
3. **Signs**. Bilateral CMO which does not respond to systemic acetazolamide.
4. **ERG** is normal.
5. **EOG** is normal to subnormal.
6. **FA** shows a flower-petal pattern of leakage at the fovea (see Fig. 13.83).
7. **Prognosis** is poor because of eventual development of geographic atrophy.

Bietti crystalline dystrophy

Bietti crystalline dystrophy is characterized by deposition of crystals in the retina and peripheral cornea.

1. **Inheritance** is XL or AR.
2. **Presentation** is in the third decade with progressive visual loss.
3. **Signs** (in chronological order)
   - Yellow-white crystals scattered throughout the posterior fundus (Fig. 15.47).
   - Localized atrophy of the RPE and choriocapillaris at the macula.
   - Diffuse atrophy of the choriocapillaris.
   - Gradual confluence and expansion of the atrophic areas into the retinal periphery.
4. **ERG** is subnormal.
5. **EOG** is subnormal.
6. **Prognosis** is variable because the rate of disease progression differs in individual cases.

Alport syndrome

Alport syndrome is a rare abnormality of glomerular basement membrane caused by mutations in several different

Fig. 15.47
Bietti crystalline dystrophy (Courtesy of J Salmon)

genes, all of which encode particular forms of type IV collagen, a major component of basement membrane. It is characterized by chronic renal failure, often associated with sensorineural deafness.

1. **Inheritance** is XL dominant.
2. **Signs**
   - Scattered, pale, yellow, punctate flecks in the perimacular area, sparing the fovea, with normal visual acuity (Fig. 15.48).
   - Larger flecks, some of which may become confluent, in the periphery (Fig. 15.49).
3. **ERG** is normal.
4. **Ocular associations** are anterior lenticonus and occasionally posterior polymorphous corneal dystrophy.
5. **Prognosis** is excellent.

Benign familial fleck retina

Benign familial fleck retina is a very rare disorder which is asymptomatic and therefore usually discovered by chance.

1. **Inheritance** is AR.
2. **Signs**
   - Widespread, discrete, yellow-white flecks at the level of the RPE which spare the fovea (Fig. 15.50).
   - The lesions have variable shapes and extend to the far periphery (Fig. 15.51).
3. **ERG** is normal.
4. **Prognosis** is excellent.

Leber congenital amaurosis

Leber congenital amaurosis is a very rare but potentially serious disease with systemic implications.

Fig. 15.48
Macular flecks in Alport syndrome (Courtesy of J. Govan)

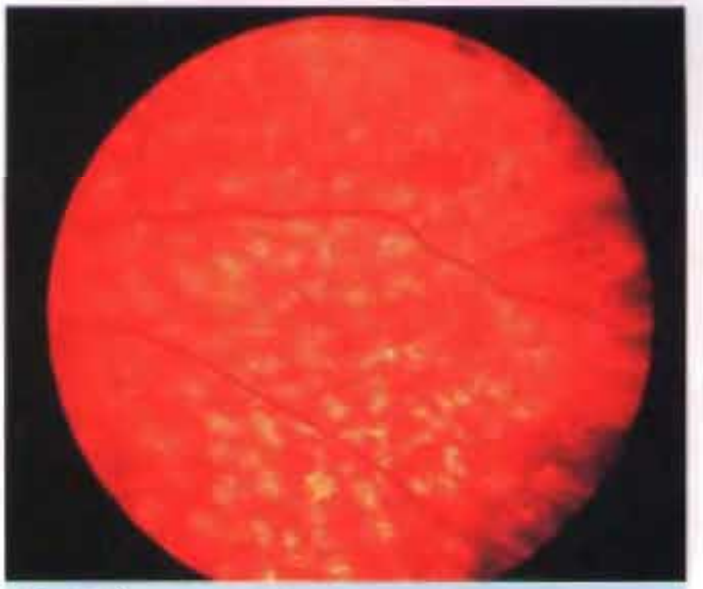


Fig. 15.49
Peripheral flecks in Alport syndrome (Courtesy of J. Govan)

Fig. 15.50
Benign familial fleck retina

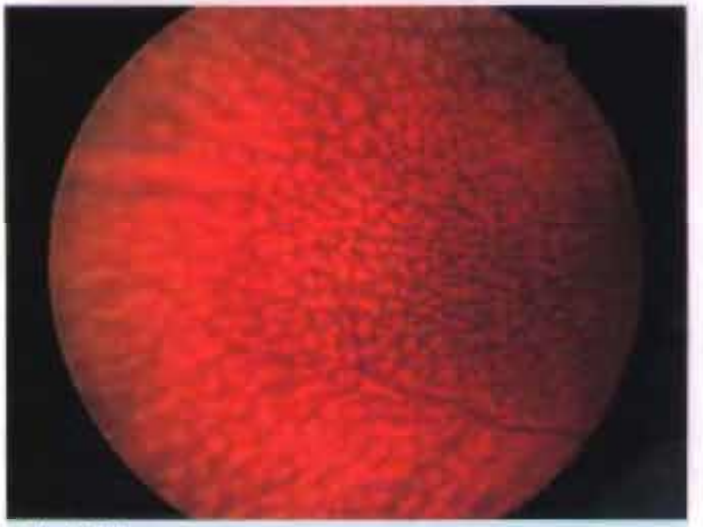


Fig. 15.51
Benign familial fleck retina

1. **Inheritance** is AR.
2. **Presentation** is with blindness at birth or within the first few years of life. Many affected children see best under bright illumination.
3. **Signs**
   - The pupillary light reflexes are absent or diminished.
   - The fundi may be initially normal despite very poor vision.
   - The most common findings are patches of peripheral chorioretinal atrophy and granularity.
   - Other findings include disc oedema, salt-and-pepper changes (Fig. 15.52), diffuse white spots, macular coloboma and bull's eye maculopathy.
   - Optic disc pallor and arteriolar attenuation develop concurrently with the retinal changes.
4. **Other ocular features**
   - Hypermetropia, keratoconus and keratoglobus.
   - Cataracts may develop by the second decade.
   - Nystagmus, roving eye movements and strabismus.
   - A characteristic feature is the oculodigital syndrome in which constant rubbing of the eyes by the child causes enophthalmos as a result of resorption of orbital fat (Fig. 15.53).
5. **ERG** is usually non-recordable even in early cases with normal fundi.
6. **Prognosis** is very poor.
7. **Systemic associations** include mental handicap, deafness, epilepsy, CNS and renal anomalies, skeletal malformations and endocrine dysfunction.

Fig. 15.53
Oculodigital syndrome (Courtesy of M. Szreter)

Congenital stationary night blindness

Normal fundus

1. **AD** congenital nyctalopia (Nougaret type) is characterized by a slightly impaired cone ERG and subnormal rod ERG.
2. **AD** stationary nyctalopia without myopia (Riggs type) is characterized by a normal cone ERG.
3. **AR or XL** congenital nyctalopia with myopia (Schubert-Bornschein type).

Abnormal fundus

1. **Oguchi disease** is an AR condition characterized by a 2–12-hour delay in attaining normal dark-adapted rod thresholds. There is an accompanying change in fundus colour from golden-brown in the light-adapted state to a normal colour in the dark-adapted state (Mizuo phenomenon).
2. **Fundus albipunctatus** is an AR condition characterized by a multitude of tiny yellow-white spots at the posterior pole, sparing the fovea (Fig. 15.54) and extending to the periphery (Fig. 15.55). The retinal blood vessels, optic disc, peripheral fields and visual acuity remain normal. The ERG and EOG may be abnormal when tested

Fig. 15.52
Leber congenital amaurosis (Courtesy of Wilmer Institute)

Fig. 15.54
Fundus albipunctatus

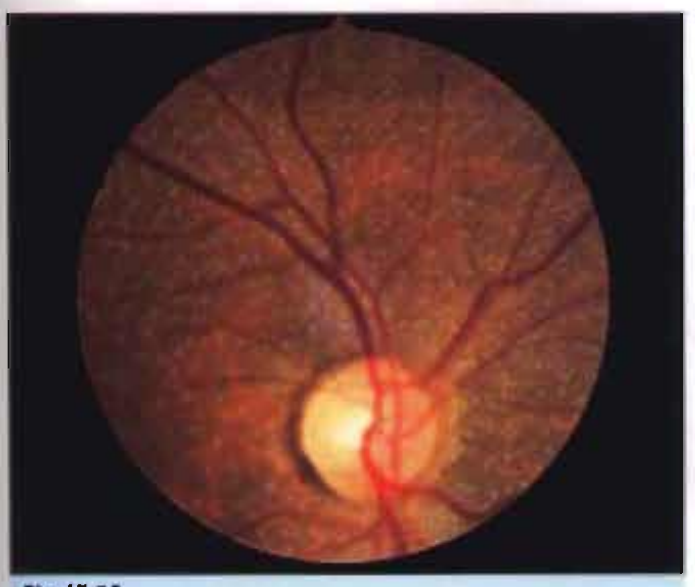


Fig. 15.55
Fundus albipunctatus

routinely but revert to normal on prolonged dark adaptation.

Congenital monochromatism

Complete rod monochromatism

1. **Inheritance** is AR.
2. **Signs**
   - Visual acuity is 6/60.
   - Macula usually appears normal but may be hypoplastic.
   - Congenital nystagmus and photophobia.
3. **ERG**. Photopic abnormal; scotopic may be subnormal; flicker fusion < 30 Hz.
4. **CV** is totally absent; all colours appear as shades of grey.

Incomplete rod monochromatism

1. **Inheritance** is AR or XL.
2. **Signs**
   - Visual acuity is 6/12–6/24.
   - Macula is usually normal.
   - Nystagmus and photophobia may be present.
3. **ERG**. Photopic abnormal; scotopic normal.
4. **CV**. Some colour vision may be present.

Cone monochromatism

1. **Inheritance** is uncertain.
2. **Signs**
   - Visual acuity is 6/6–6/9.
   - Normal macula.
   - Nystagmus and photophobia are absent.
3. **ERG** is normal.
4. **CV** is totally absent.

Choroidal dystrophies

Choroideremia

Choroideremia is a very rare condition which only affects males.

1. **Inheritance** is XL recessive with the gene locus on Xq21. This has the following implications:
   - All daughters of affected fathers will be carriers.
   - Half of the sons of female carriers will develop the disease.
   - Half of the daughters of female carriers will also be carriers.
   - An affected male cannot transmit the gene to his sons.
2. **Female carriers** show mild, usually innocuous, patchy peripheral atrophy and mottling of the RPE (Fig. 15.56). However, visual acuity, peripheral fields and ERG are normal.
3. **Presentation** is in the first decade with nyctalopia.
4. **Signs** (in chronological order)
   - Mid-peripheral patches of choroidal and RPE atrophy (Fig. 15.57).
   - Diffuse atrophy of the choriocapillaris and RPE with preservation of the intermediate and large choroidal vessels (Fig. 15.58).
   - Atrophy of intermediate and large choroidal vessels rendering visible the underlying sclera (Fig. 15.59).

> ***NB:*** In contrast to primary retinal dystrophies, the fovea is spared until late (Fig. 15.60a) and the optic disc and retinal blood vessels remain relatively normal.

5. **ERG**. Scotopic ERG is non-recordable; photopic is severely subnormal.
6. **EOG** is subnormal.
7. **FA** of the intermediate stage of choroideremia shows filling of the retinal and large choroidal vessels but not of the choriocapillaris. There is also hypofluorescence

Fig. 15.56
Peripheral changes in a carrier of choroideremia

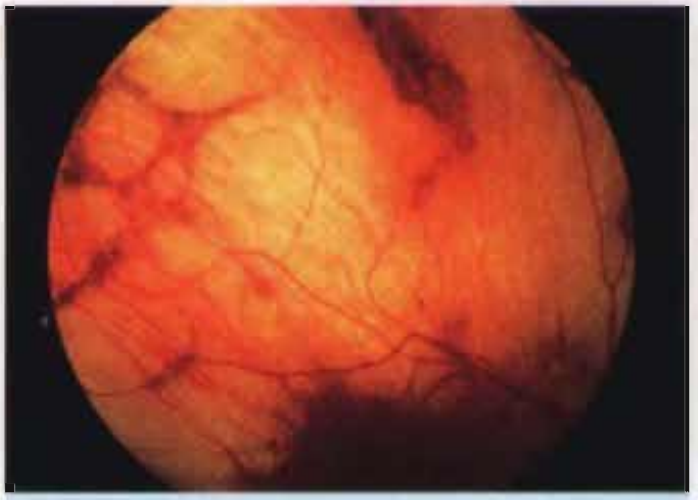


Fig. 15.57
Mid-peripheral changes in choroideremia (Courtesy of K. Jordan)

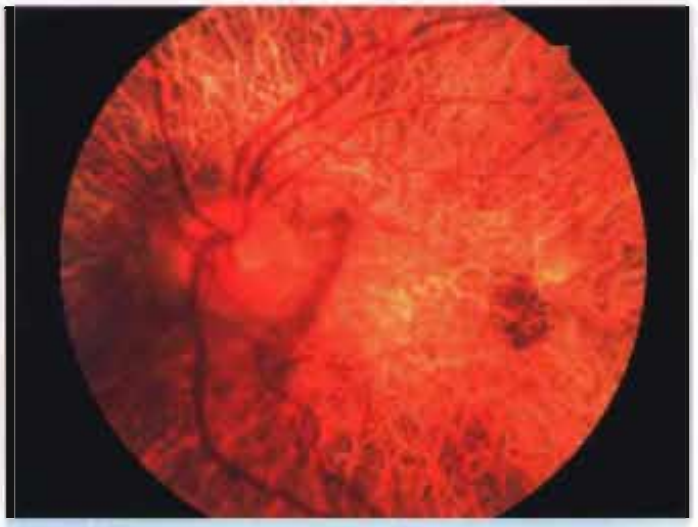


Fig. 15.58
Choroideremia with preservation of intermediate and large choroidal vessels

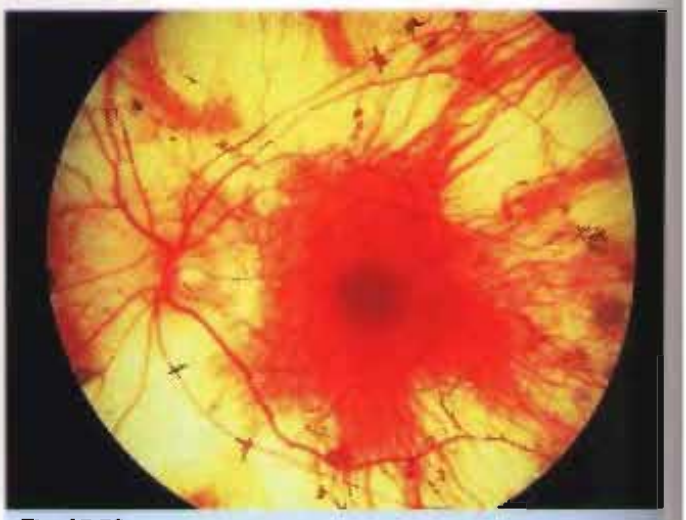


Fig. 15.59
Advanced choroideremia (Courtesy of K. Nischal)

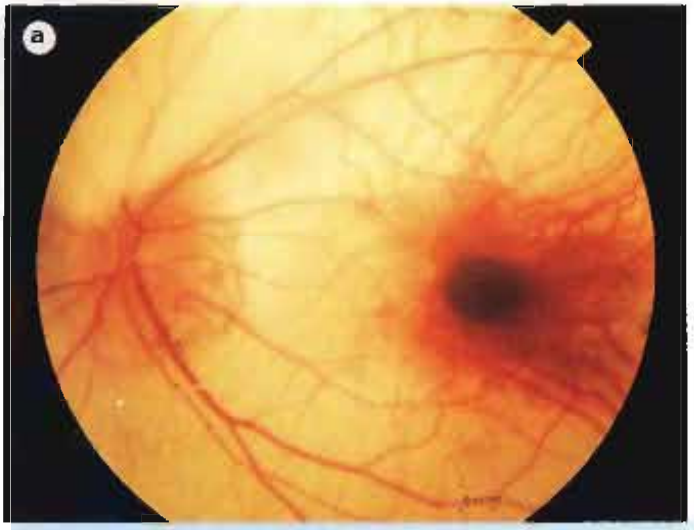
corresponding to the intact fovea and a surrounding area of hyperfluorescence due to a window defect (Fig. 15.60b).

8. **Prognosis** is very poor; although most patients retain useful vision until the sixth decade, very severe visual loss occurs thereafter.

Gyrate atrophy

Gyrate atrophy of the choroid and retina is caused by mutations of the gene encoding the main ornithine degradation enzyme, ornithine keto-acid aminotransferase. Deficiency of the enzyme leads to elevated ornithine levels in the plasma, urine, CSF and aqueous humour.

1. **Inheritance** is AR.
2. **Presentation** is in the second decade with axial myopia and nyctalopia.
3. **Signs** (in chronological order)
   - Peripheral patches of chorioretinal atrophy (Fig. 15.61) and vitreous degeneration.



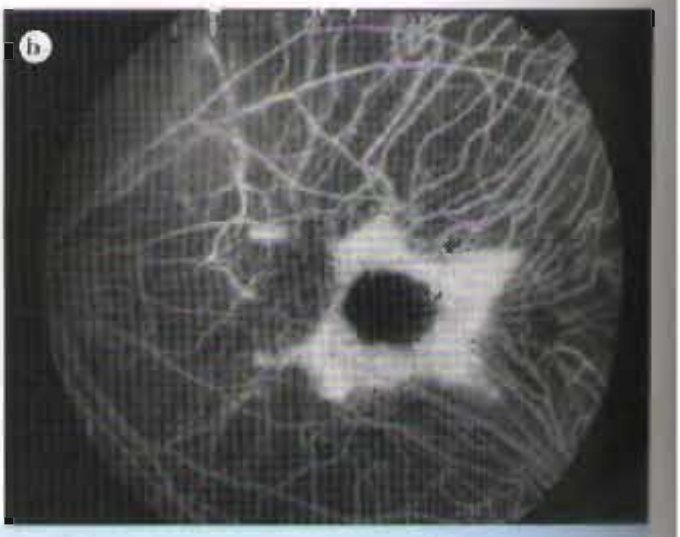


Fig. 15.60
(a) End-stage choroideremia; (b) FA showing diffuse loss of the choriocapillaris with preservation of the fovea (Courtesy of S. Milewski)

- Confluence of lesions forming a scalloped posterior border (Fig. 15.62).
- Gradual peripheral and central spread, sparing the fovea until late (Figs 15.63 and 15.64a).

NB: In contrast to choroideremia there is extreme attenuation of retinal blood vessels.

4. **ERG** is abnormal and later extinguished.
5. **EOG** is subnormal in late disease.
6. **FA** shows the sharp contrast between normal and atrophic areas (Fig. 15.64b).
7. **Prognosis** is poor with legal blindness occurring in the fourth to sixth decades from geographic atrophy, although vision may fail earlier due to cataract, CMO or epiretinal membrane formation.
8. **Treatment.** There are two clinically different subtypes of gyrate atrophy based on response to pyridoxine (vitamin B_6), which may normalize plasma and urinary ornithine levels. Patients responsive to vitamin B_6 generally have a less severe and more slowly progressive clinical course than those who

Fig. 15.62
Coalescent gyrate atrophy

Fig. 15.61
Peripheral patches of gyrate atrophy

Fig. 15.63
Advanced gyrate atrophy

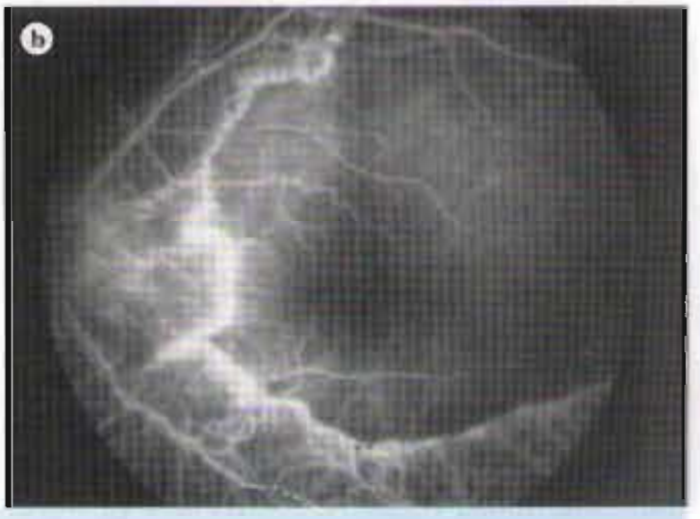


Fig. 15.64
(a) Gyrate atrophy; (b) FA showing sharp contrast between normal and atrophic areas (Courtesy of S. Milewski)

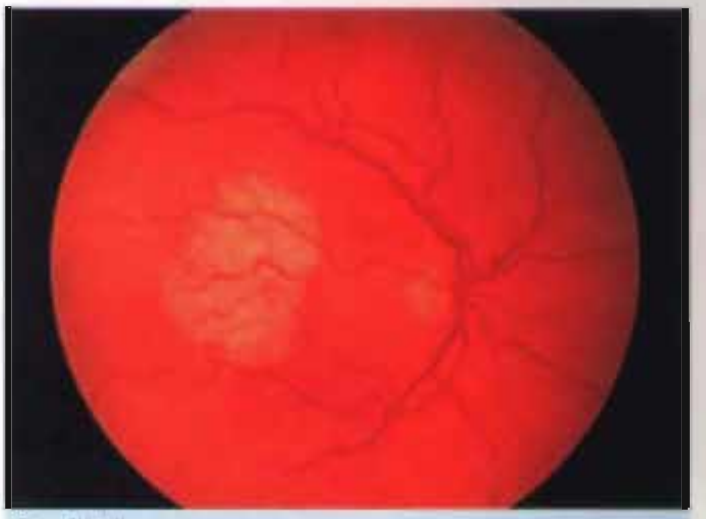


Fig. 15.65
Central areolar choroidal dystrophy

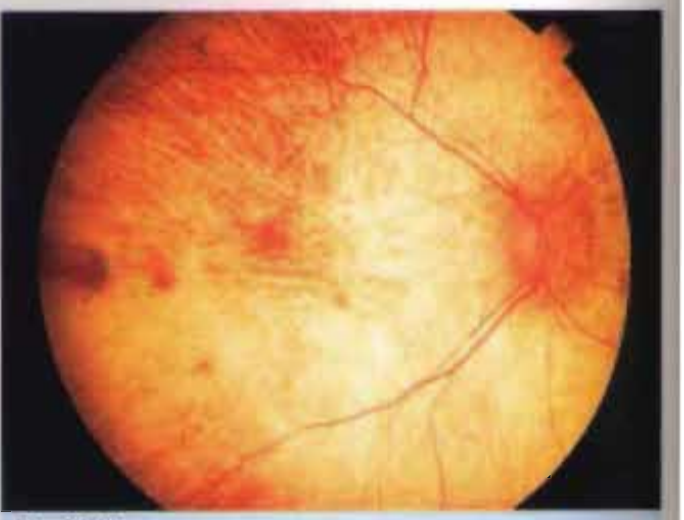


Fig. 15.66
Diffuse choroidal atrophy (Courtesy of S. Milewski)

are not. Reduction in ornithine levels with an arginine-restricted diet is also beneficial in slowing progression.

Central areolar choroidal dystrophy

1. **Inheritance** is AD with the gene locus on 17p.
2. **Presentation** is in the third to fourth decades with gradual, bilateral impairment of central vision.
3. **Signs** (in chronological order)
   - Non-specific foveal granularity.
   - Circumscribed RPE atrophy and loss of the choriocapillaris at the macula.
   - Slowly expanding geographic atrophy within which the larger choroidal vessels are prominent (Fig. 15.65).
4. **ERG** is normal.
5. **EOG** is normal.
6. **Prognosis** is poor with severe visual loss occurring by the sixth to seventh decades.

Diffuse choroidal atrophy

1. **Inheritance** is AD.
2. **Presentation** is in the fourth to fifth decades with impairment of central vision or nyctalopia.
3. **Signs** (in chronological order)
   - Parapapillary and pericentral atrophy of the RPE and choriocapillaris.
   - Gradual enlargement until the entire fundus is affected.
   - Atrophy of most of the larger choroidal vessels with scleral visibility (Fig. 15.66).
   - The retinal vessels may be normal or slightly constricted.
4. **ERG** is subnormal.
5. **Prognosis** is poor because of early macular involvement.

Helicoidal parapapillary chorioretinal degeneration

1. **Inheritance** is AD.
2. **Presentation** is in childhood.
3. **Signs**
   - Bilateral, slowly-enlarging, tongue-like, well-defined strips of chorioretinal atrophy radiating from the optic nerve head (Fig. 15.67).
   - Separate, peripheral, circular lesions may be present.
4. **ERG** ranges from normal to severely abnormal.
5. **Prognosis** is variable as severe disease may be seen in the young and mild disease in the elderly.

Pigmented paravenous retinochoroidal atrophy

Pigmented paravenous retinochoroidal atrophy is a rare condition, usually discovered incidentally in young men.

1. **Inheritance.** No distinctive pattern has been established although AD, AR, XL and even YL transmissions have been proposed.
2. **Signs**
   - Bilateral, bone corpuscular pigment accumulation along major retinal veins.
   - Adjacent, sharply outlined zones of chorioretinal atrophy which may surround the disc (Fig. 15.68).
3. **ERG** is usually normal.
4. **Prognosis** is excellent because macular involvement is rare.

Vitreoretinopathies

Congenital retinoschisis

Congenital retinoschisis is characterized by bilateral maculopathy, associated with peripheral retinoschisis in 50% of patients. The basic defect is in the Müller cells, causing splitting of the retinal nerve fibre layer from the rest of the sensory retina. This differs from acquired retinoschisis in which splitting occurs at the outer plexiform layer.

Fig. 15.67
Helicoid chorioretinal degeneration

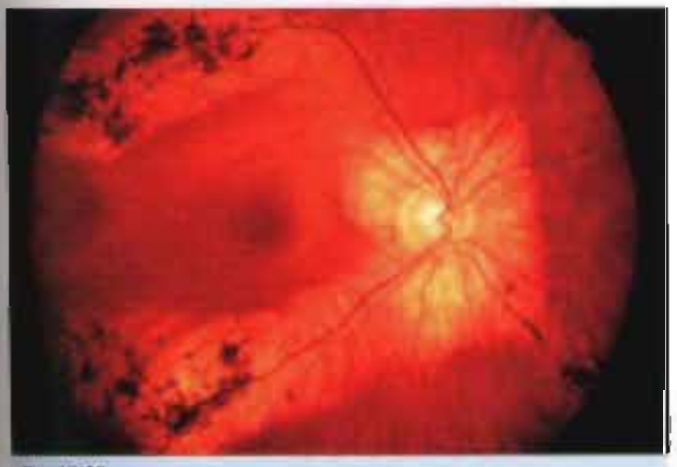


Fig. 15.68
Pigmented paravenous chorioretinal atrophy (Courtesy of C Barry)

1. **Inheritance** is XL with the gene designated RS1.
2. **Presentation** is between the ages of 5 and 10 years with reading difficulties due to maculopathy. Less frequently the disease presents in infancy with squint or nystagmus associated with advanced peripheral retinoschisis often with vitreous haemorrhage.
3. **Signs**
   a. ***Foveal schisis*** is characterized by tiny cystoid spaces with a 'bicycle-wheel' pattern of radial striae (Fig. 15.69) more apparent when examined under red-free light. Over time the radial folds become less evident, leaving a blunted foveal reflex (*see* Fig. 15.73a).
   b. ***Peripheral schisis*** predominantly involves the infero-temporal quadrant, does not extend but may undergo the following secondary changes:

Fig. 15.69
'Bicycle wheel-like' maculopathy in congenital retinoschisis (Courtesy of P. Morse)

- The inner layer, which consists only of the internal limiting membrane and the retinal nerve fibre layer, may develop oval defects (Figs 15.70 and 15.71).
- In extreme cases, the defects coalesce, leaving only retinal blood vessels floating in the vitreous ('vitreous veils').

   c. ***Other signs*** include perivascular sheathing, a golden glistening of the peripheral retina, nasal dragging of retinal vessels, retinal flecks, subretinal exudates and neovascularization.
4. **Complications** include vitreous and intra-schisis haemorrhage, and retinal detachment.
5. **ERG** is normal in eyes with isolated maculopathy. Eyes with peripheral schisis show a characteristic selective

Fig. 15.70
Defect in the inner leaf of congenital retinoschisis

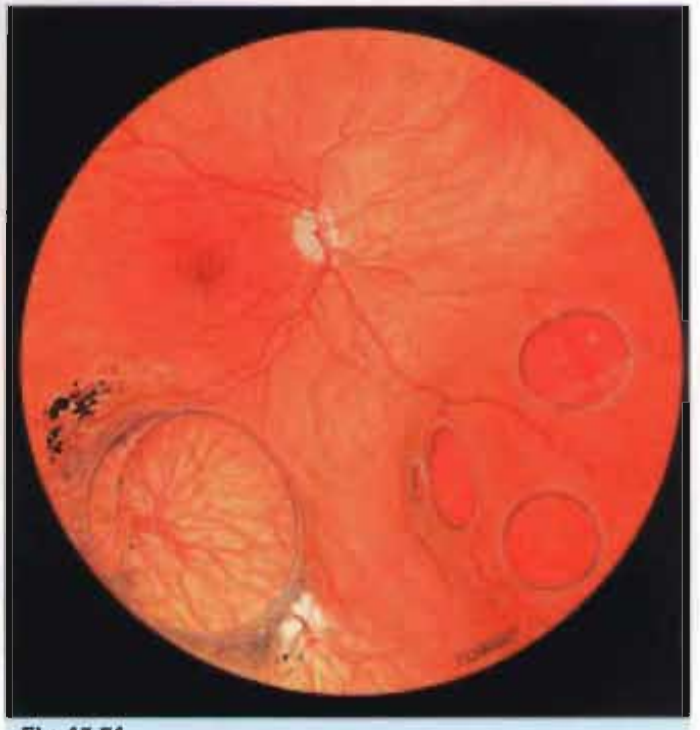


Fig. 15.71
Large defects in the inner leaf of congenital retinoschisis

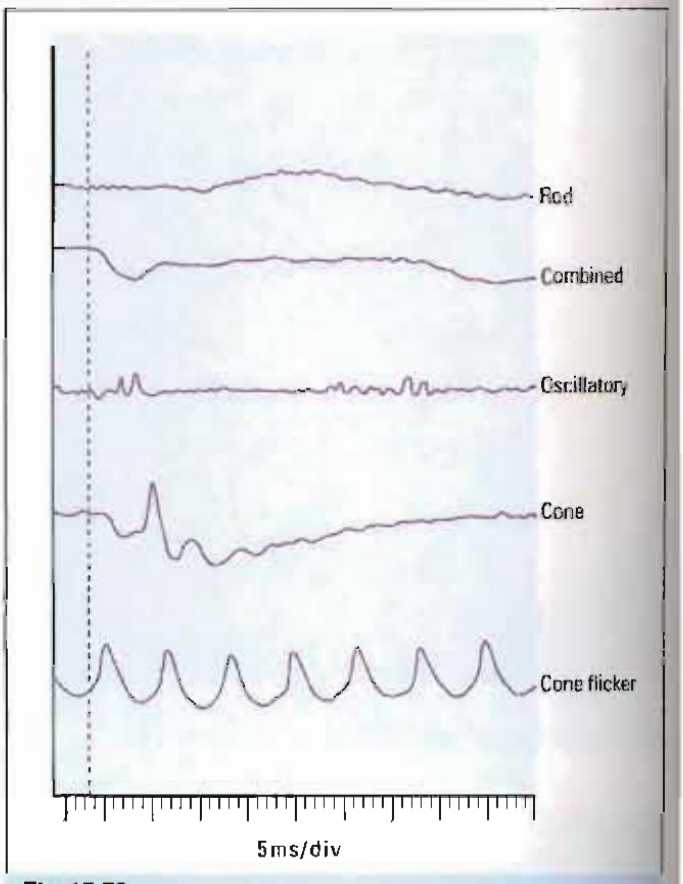


Fig. 15.72
Electroretinogram in congenital retinoschisis *(see text)*

decrease in b-wave amplitude as compared with a-wave amplitude on scotopic and photopic testing (Fig. 15.72).

6. **EOG** is normal in eyes with isolated maculopathy but subnormal in eyes with advanced peripheral lesions.
7. **CV** shows tritan defect.
8. **FA** of maculopathy may show mild window defects but no leakage (Fig. 15.73b).
9. **Visual fields** in eyes with peripheral schisis show corresponding absolute defects.
10. **Prognosis** is poor due to progressive maculopathy. Visual acuity deteriorates during the first two decades and may then remain stable until the fifth or sixth decade when it further deteriorates. Patients with peripheral schisis may have sudden visual loss at any time due to haemorrhage or retinal detachment.

Stickler syndrome

Stickler syndrome (hereditary arthro-ophthalmopathy) is a disorder of collagen connective tissue, resulting in abnormal vitreous, myopia, and a variable degree of orofacial abnor-

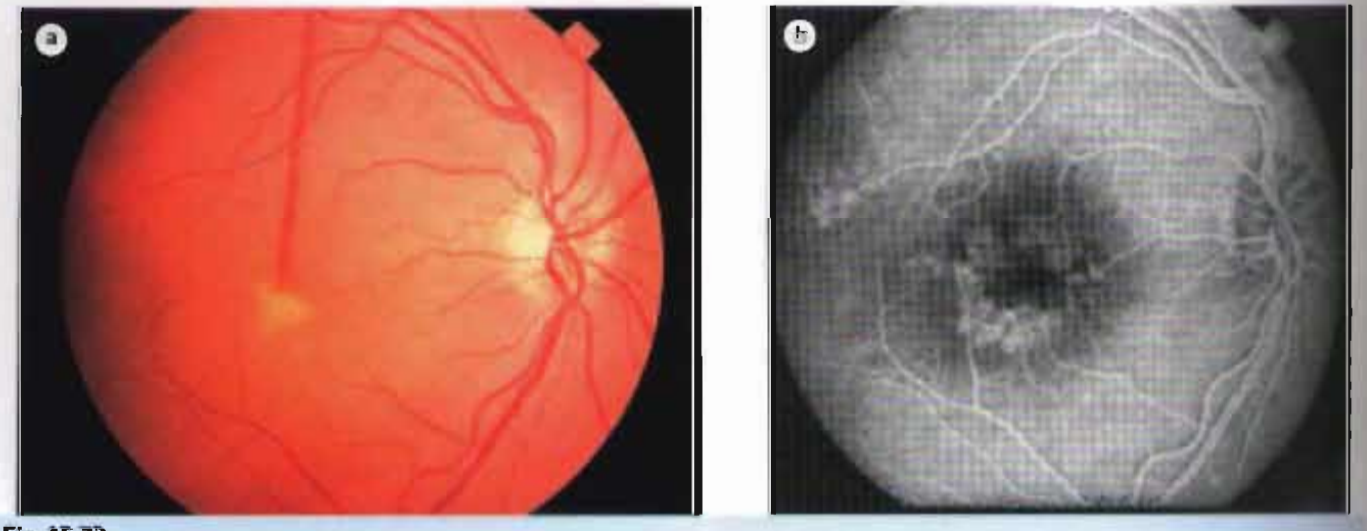


Fig. 15.73
(a) Late-stage maculopathy in congenital retinoschisis; (b) FA showing window defects

mality, deafness and arthropathy. It is the commonest inherited cause of retinal detachment in children.

1. **Inheritance** is AD with complete penetrance but variable expressivity.
2. **Signs**
   - An optically empty vitreous cavity due to liquefaction and syneresis.
   - Circumferential, equatorial, translucent membranes extending a short way into the vitreous cavity (Fig. 15.74).
   - Radial lattice-like degeneration associated with RPE hyperplasia, vascular sheathing and sclerosis (Fig. 15.75).
3. **Complications.** Retinal detachment, often bilateral, develops in approximately 30% of cases due to multiple or giant tears. Because the prognosis is poor, patients should be examined regularly and retinal breaks treated prophylactically.

Fig. 15.74
Empty vitreous in Stickler syndrome

Fig. 15.75
Radial lattice degeneration and pigmentary changes in Stickler syndrome

4. **Associations**
   a. ***Congenital high myopia*** is very common.
   b. ***Presenile cataract***, in 50% of cases, is characterized by peripheral cortical wedge-shaped opacities, which are frequently non-progressive.
   c. ***Ectopia lentis*** in about 10%.
   d. ***Glaucoma*** in 10% of cases due to an angle anomaly similar to that seen in Marfan syndrome.
5. **Systemic features**
   a. ***Facial*** anomalies include a flattened nasal bridge and maxillary hypoplasia.
   b. ***Skeletal*** involvement includes a marfanoid habitus, arthropathy and joint hyperextensibility.
   c. ***Robin sequence*** is characterized by micrognathia, glossoptosis, cleft soft palate and high-arched palate.
   d. ***Other*** features include deafness and mitral valve prolapse.
6. **Differential diagnosis.** Wagner syndrome has ocular similarities with Stickler. However, it is not associated with systemic disease, myopia is mild and retinal detachment is uncommon.

Favre–Goldmann syndrome

Favre–Goldmann syndrome has features of retinoschisis and pigmentary retinopathy.

1. **Inheritance** is AR.
2. **Presentation** is in childhood with nyctalopia.
3. **Signs**
   - Vitreous shows syneresis but the cavity is not optically 'empty'.
   - Retinal lesions are similar to congenital retinoschisis, although the macular findings are more subtle.
   - Pigmentary retinopathy (similar to RP) and white, dendritiform, arborescent peripheral retinal vessels (Fig. 15.76).
4. **ERG** is subnormal.
5. **Prognosis** is poor.

Familial exudative vitreoretinopathy

Familial exudative vitreoretinopathy (Criswick–Schepens syndrome) is a slowly progressive condition characterized by avascularity of the temporal retinal periphery, similar to retinopathy of prematurity, but not associated with low birth weight and prematurity.

1. **Inheritance** is AD and rarely XL recessive with high penetrance and variable expressivity.
2. **Presentation** is in late childhood.
3. **Signs** (in chronological order)
   - Vitreous degeneration and peripheral vitreoretinal attachments associated with areas of 'white without pressure'.
   - Peripheral vascular tortuosity, telangiectasia (Fig. 15.77), neovascularization, haemorrhages and subretinal exudates.

Fig. 15.76
Peripheral dendritiform lesions in Favre–Goldmann syndrome
(Courtesy of Moorfields Eye Hospital)

- Fibrovascular proliferation (Fig. 15.78) and vitreoretinal traction resulting in ridge formation (Fig. 15.79), vascular straightening, localized retinal detachment and temporal dragging of the macula (Fig. 15.80).
- Extensive tractional retinal detachment, massive subretinal exudation, band keratopathy, cataract and glaucoma.

4. **ERG** is normal.
5. **FA** shows peripheral retinal non-perfusion and highlights straightening of blood vessels (Fig. 15.81).
6. **Prognosis** is poor although in some cases peripheral retinal laser photocoagulation or cryotherapy may be beneficial. Vitreoretinal surgery for retinal detachment is difficult but may be successful in selected cases.

Fig. 15.77
Telangiectasia in familial exudative vitreoretinopathy

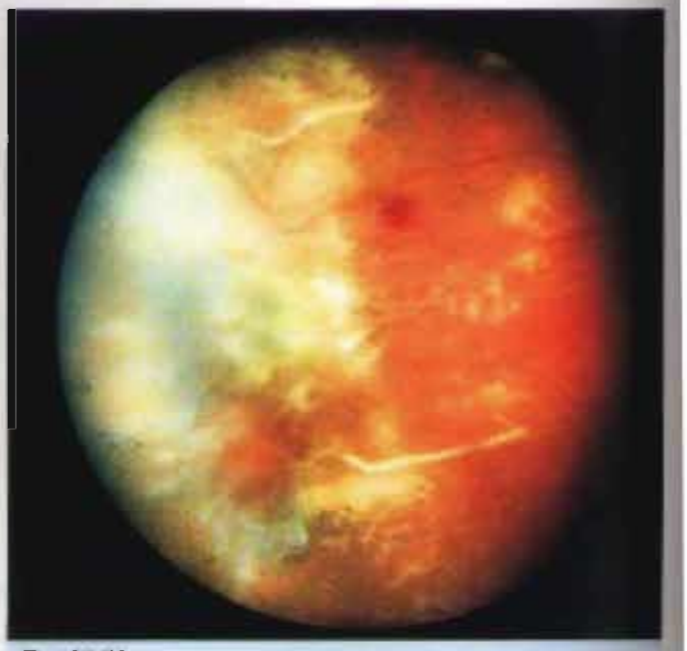


Fig. 15.78
Fibrovascular proliferation in familial exudative vitreoretinopathy

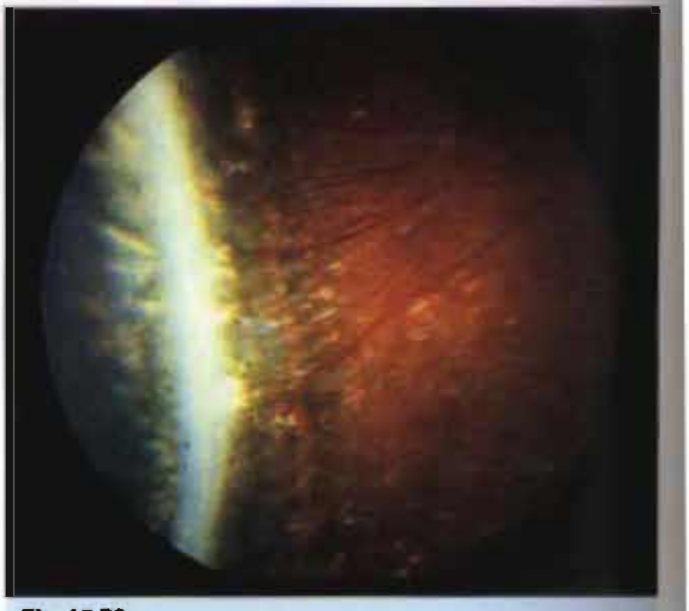


Fig. 15.79
Fibrovascular ridge in familial exudative vitreoretinopathy

Erosive vitreoretinopathy

1. **Inheritance** is AD.
2. **Presentation** is in early life.
3. **Signs**
   - Vitreous syneresis and multiple foci of vitreoretinal traction.
   - Thinning of the RPE and progressive choroidal atrophy which may eventually involve the macula and resemble choroideremia.
4. **Complications**. Retinal detachment in 70%, often bilateral and caused by giant tears.

Fig. 15.80
'Dragging' of the macula in familial exudative vitreoretinopathy

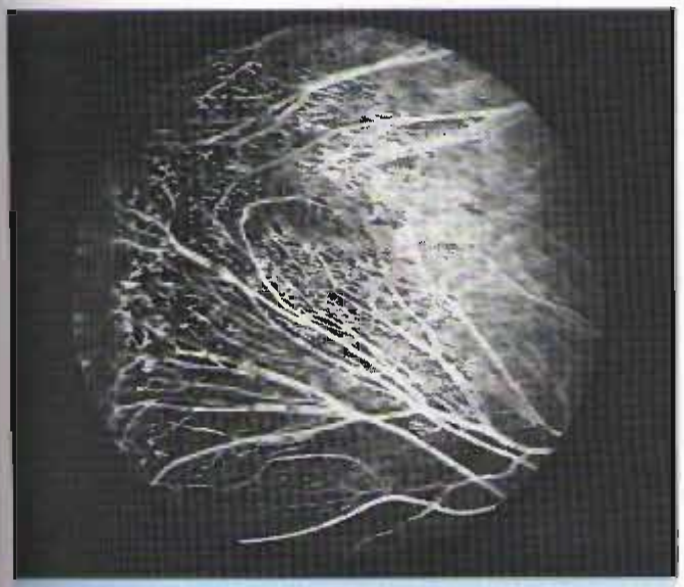


Fig. 15.81
FA in familial exudative vitreoretinopathy showing abrupt termination of peripheral retinal vasculature

5. **ERG** is subnormal.
6. **Prognosis** is guarded because retinal detachment may be difficult to treat.

Dominant neovascular inflammatory vitreoretinopathy

1. **Inheritance** is AD.
2. **Presentation** is in the second to third decades with vitreous floaters.
3. **Signs**
   - Uveitis.
   - Pigmentary retinal degeneration.
   - Peripheral vascular closure and neovascularization.
4. **Complications** include vitreous haemorrhage, tractional retinal detachment and cystoid macular oedema.
5. **ERG** shows selective loss of b-wave amplitude.
6. **Prognosis** is guarded. Peripheral retinal photocoagulation and vitreous surgery may be required to preserve vision.

Dominant vitreoretinochoroidopathy

1. **Inheritance** is AD.
2. **Presentation** is in adult life if symptomatic, but frequently the condition is discovered by chance.
3. **Signs**
   - An encircling band of pigmentary disturbance between the ora serrata and equator with a sharply defined posterior border.
   - Within the band there is arteriolar attenuation, neovascularization, punctate white opacities and later chorioretinal atrophy.
4. **Complications**, which are uncommon, include cystoid macular oedema and occasionally vitreous haemorrhage.
5. **ERG** is subnormal.
6. **Prognosis** is good.

Albinism

Albinism is a genetically determined heterogeneous group of disorders involving hypopigmentation of the eyes and/or skin, due to a deficiency of tyrosinase, which mediates the conversion of tyrosine to melanin. The two types are (a) *oculocutaneous* and (b) *ocular*. The former may be tyrosinase-negative or tyrosinase-positive and is inherited as AR, while the latter is commonly XL.

Oculocutaneous albinism

Tyrosinase-negative

These albinos are incapable of synthesizing melanin and have blond hair and very pale skin (Fig. 15.82).

1. **Iris** is diaphanous and translucent (Fig. 15.83), giving rise to a 'pink-eyed' appearance.
2. **Fundus** (Fig. 15.84).
   - Lack of pigment with conspicuously large choroidal vessels.
   - Hypoplasia of vessels forming the perimacular arcades.
   - Foveal and optic nerve hypoplasia may be present.
3. **Refractive errors** are common and visual acuity is usually <6/60.
4. **Nystagmus** is usually pendular and horizontal, and increases on bright illumination. Its severity may lessen with age.

5. **The chiasm** has a decreased number of uncrossed nerve fibres. Abnormal visual pathways also exist from the lateral geniculate body to the occipital cortex.

Tyrosinase-positive

These albinos can synthesize variable amounts of melanin and vary in complexion from very fair to almost normal.

1. **Iris** may be blue or dark-brown with variable translucency (Fig. 15.85).
2. **Fundus** shows variable hypopigmentation (Fig. 15.86).
3. **Visual acuity** is usually impaired due to foveal hypoplasia.
4. **Associated syndromes**
   a. *Chediak–Higashi syndrome* is associated with white cell abnormalities resulting in recurrent pyogenic infections and an early demise.

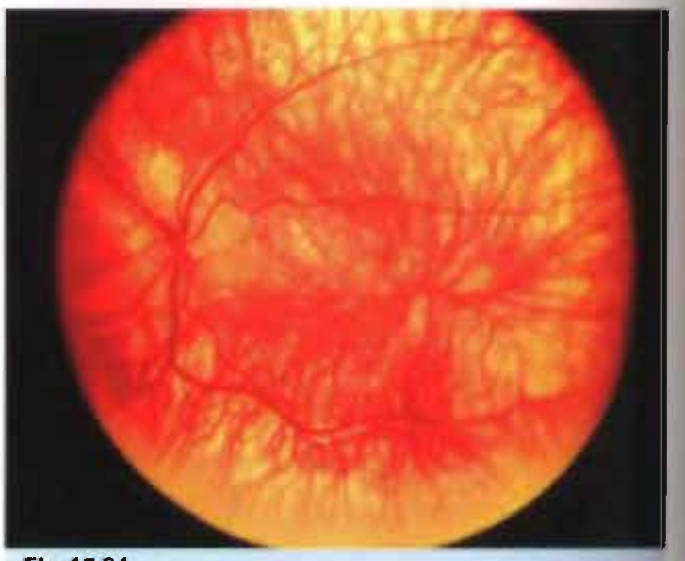


Fig. 15.84
Severe fundus hypopigmentation in tyrosinase-negative oculocutaneous albinism (Courtesy of K. Nischal)

Fig. 15.82
Blond hair and pink-eyed appearance in tyrosinase-negative oculocutaneous albinism

Fig. 15.85
Partial iris transillumination in tyrosinase-positive albinism

Fig. 15.83
Iris transillumination in tyrosinase-negative oculocutaneous albinism

   b. *Hermansky–Pudlak syndrome* is a lysosomal storage disease of the reticuloendothelial system characterized by easy bruising due to platelet dysfunction.

Ocular albinism

The eyes are predominantly affected, with less evident skin and hair involvement.

1. **Inheritance** is XL or, less commonly, AR.
2. **Female carriers** are asymptomatic and have normal vision, although they may show partial iris translucency, macular stippling and scattered areas of depigmentation and granularity in the mid-periphery (Fig. 15.87).
3. **Affected males** manifest hypopigmented irides and fundi.

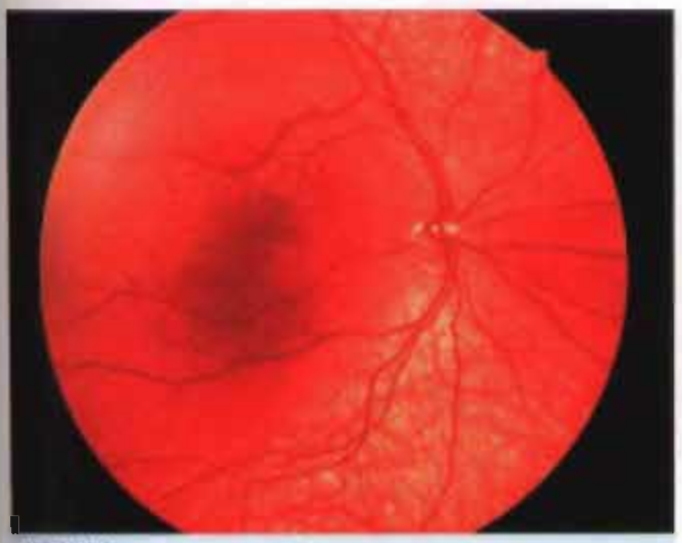


Fig. 15.86
Mild fundus hypopigmentation in tyrosinase-positive albinism

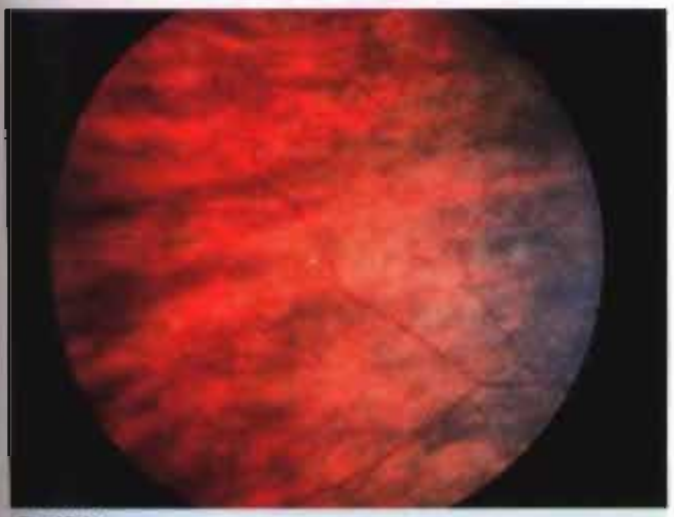


Fig. 15.87
Peripheral fundus changes in a female carrier of X-linked ocular albinism

Cherry-red spot at macula

The cherry-red spot at the macula is a clinical sign seen in the context of thickening and loss of transparency of the retina at the posterior pole. The foveola, being the thinnest part of the retina and devoid of ganglion cells, retains relative transparency, due to which the colour of the choroid shines through. This striking retinal lesion, commonly seen in occlusion of the central retinal artery, is additionally a feature of a rare group of inherited metabolic diseases which comprise the sphingolipidoses. These diseases are characterized by the progressive intracellular storage of excessive quantities of certain glycolipids and phospholipids in various tissues of the body, including the retina. The lipids are stored in the ganglion cell layer of the retina, giving the retina a white appearance. As ganglion cells are absent at the foveola, this area retains relative transparency and contrasis with the surrounding opaque retina (Fig. 15.88). With the passage of time the ganglion cells die and the spot becomes less evident. The late stage of the disease is characterized by atrophy of the retinal nerve fibre layer and consecutive optic atrophy. Systemic associations are as follows:

Fig. 15.88
Cherry-red spot at the macula in Tay–Sachs disease

1. **Tay–Sachs disease** (Gm2 gangliosidosis type 1), also called infantile amaurotic familial idiocy, is an autosomal recessive disease with an onset during the first year of life, usually ending in death before the age of 2 years. It typically affects European Jews and is characterized by progressive neurological disease and eventual blindness. A cherry-red spot is present in about 90% of cases.
2. **Niemann–Pick disease** is divided on a clinical and chemical basis into the following four groups:
   a. Group A with severe early CNS deterioration.
   b. Group B with normal CNS function.
   c. Group C with moderate CNS involvement and a slow course.
   d. Group D with a late onset and eventual severe CNS involvement.
   The incidence of a cherry-red spot is lower than in Tay–Sachs disease.
3. **Sandhoff disease** (Gm2 gangliosidosis type 2) is almost identical to Tay–Sachs disease.
4. **Generalized gangliosidosis** (Gm1 gangliosidosis type 1) is characterized by hypoactivity, oedema of the face and extremities, and skeletal anomalies from birth.
5. **Sialidosis types 1 and 2** (cherry-red spot myoclonus syndrome) are characterized by myoclonic jerks, pain in the limbs and unsteadiness. A cherry-red spot may be the initial finding.

CHAPTER 16

Strabismus

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Introduction

Definitions

Normal ocular alignment involves parallelism of the visual axes for distance vision, or intersection of the visual axes at the point of fixation for near.

1. **Strabismus** (squint) is a misalignment of the eyes.
2. **Orthophoria** implies perfect ocular alignment *without effort*, even in the absence of any stimulus for fusion. It is rare; most individuals manifest mild heterophoria.
3. **Heterophoria** ('phoria) implies a tendency of the eyes to deviate (latent squint). Ocular alignment is maintained with effort.
4. **Heterotropia** ('tropia) implies a manifest squint—the eyes are misaligned. A phoria may become a tropia if:
   - Muscle strength is inadequate to maintain ocular alignment.
   - Stimulus for fusion is weak (e.g. uniocular blurred vision).
   - Neurological pathways subserving ocular coordination break down.
5. **Prefixes** 'eso' and 'exo' imply inward and outward ocular deviations respectively. For example: an exophoria is a tendency of the eyes to diverge, while esotropia is a manifest convergent squint. Ocular misalignment may also be vertical, where the prefixes hypo- (downward) and hyper- (upward) apply, or torsional.
6. **Visual axis** (line of vision) passes from the fovea, through the nodal point of the eye to the point of fixation (object of regard). The two visual axes normally intersect at the point of fixation. The fovea is usually slightly temporal to the posterior pole (geometrical centre at the back of the globe); the visual axis therefore cuts the cornea slightly nasal of centre.
7. **Anatomical axis** is a line passing from the posterior pole through the centre of the cornea.
8. **Angle kappa** is the angle subtended by the visual and anatomical axes and is usually about 5° (Fig. 16.1). Angle kappa is positive when the fovea is temporal to the posterior pole, and negative when the converse applies. Abnormalities of angle kappa may result in pseudostrabismus (*see* later).

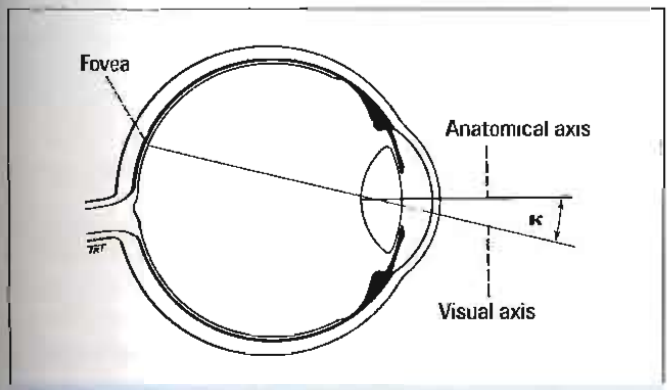

Fig. 16.1
Angle kappa

Anatomy of extraocular muscles

General principles

The lateral and medial orbital walls are at an angle of 45° to each other (Fig. 16.2a). The orbital axis therefore forms an angle of 22.5° with both lateral and medial walls. For the sake of simplicity this angle is usually regarded as being 23°. When the eye is looking straight ahead at a fixed point on the horizon with the head erect (primary position of gaze), the visual axis forms an angle of 23° with the orbital axis (Fig. 16.2b). The actions of the extraocular muscles depend on the position of the globe at the time of muscle contraction.

1. **Primary action** of a muscle is its major effect when the eye is in the primary position.
2. **Subsidiary actions** are the additional effects on the position of the eye.
3. **Listing plane** is an imaginary coronal plane passing through the centre of rotation of the globe. The globe rotates on the axes of Fick, which intersect in Listing plane (Fig. 16.3).
   - The globe rotates left and right on the vertical Z-axis.
   - The globe moves up and down on the horizontal X-axis.

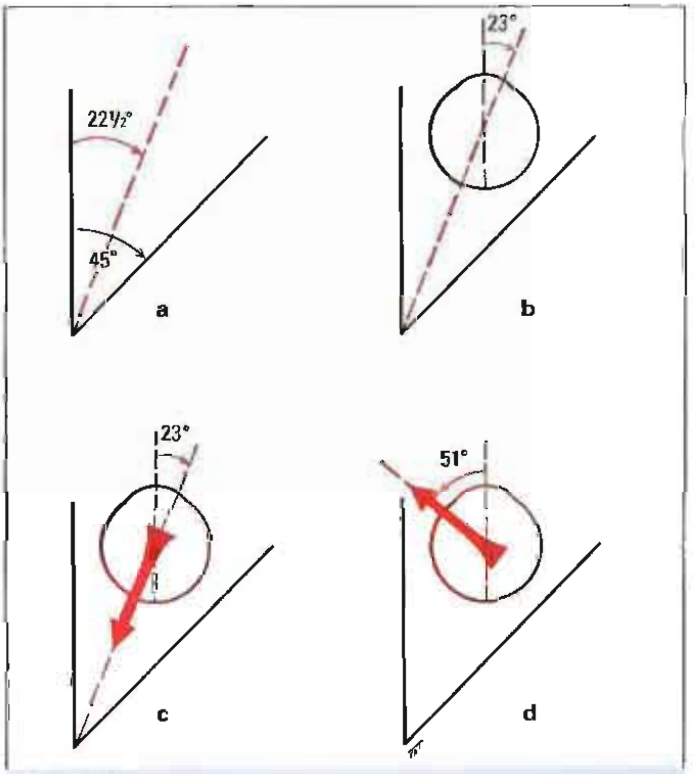

Fig. 16.2
Anatomy of extraocular muscles (see text)

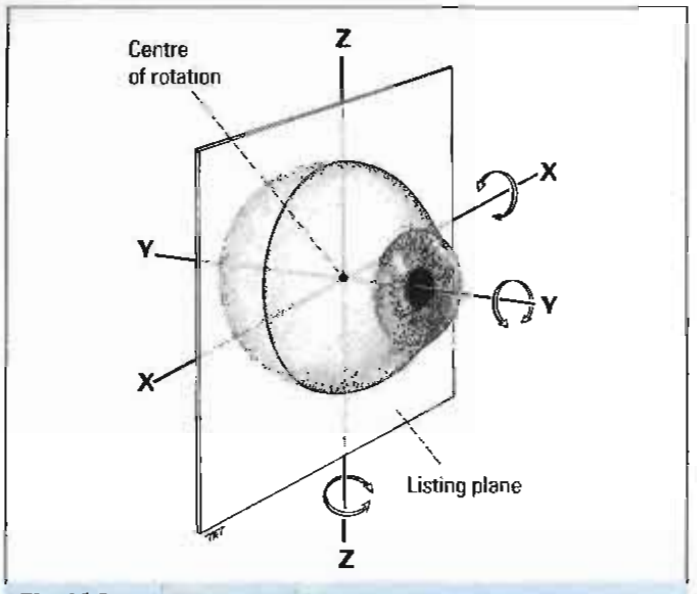

Fig. 16.3
Listing plane and axes of Fick (see text)

- Torsional movements occur on the *Y*-axis which traverses the globe from front to back (similar to the anatomical axis of the eye).

Horizontal rectus muscles

When the eye is in the primary position, the horizontal recti are purely horizontal movers on the vertical Z-axis and have only primary actions.

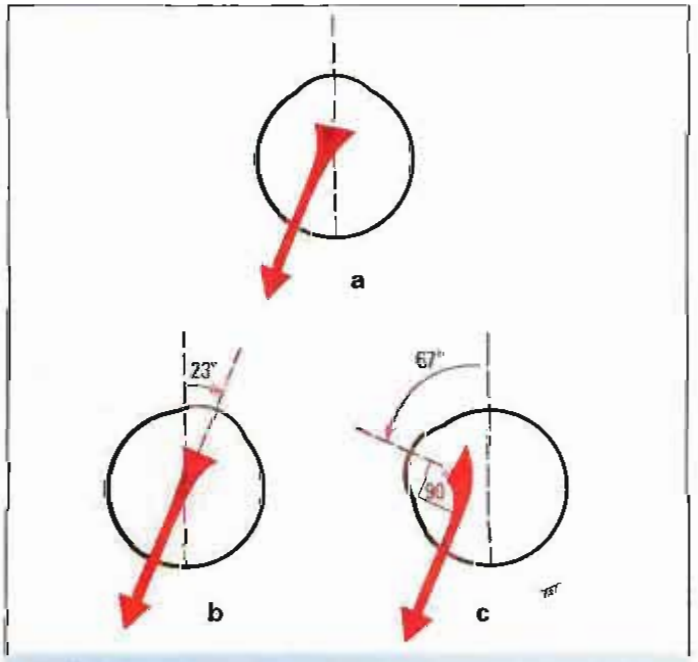

Fig. 16.4
Actions of the right superior rectus muscle

1. **Medial rectus** originates at the annulus of Zinn at the orbital apex and inserts 5.5 mm behind the nasal limbus. Its sole action is adduction.
2. **Lateral rectus** originates at the annulus of Zinn and inserts 6.9 mm behind the temporal limbus. Its sole action is abduction.

Vertical rectus muscles

The vertical recti run in line with the orbital axis and are inserted in front of the equator. They therefore form an angle of 23° with the visual axis (*see* Fig. 16.2c).

1. **Superior rectus** originates from the upper part of the annulus of Zinn and inserts 7.7 mm behind the superior limbus.
   - The primary action of the superior rectus is elevation (Fig. 16.4a). Secondary actions are adduction and intorsion.
   - When the globe is abducted 23°, the visual and orbital axes coincide (Fig. 16.4b). In this position it has no subsidiary actions and can only act as an elevator. This is therefore the optimal position of the globe for testing the function of the superior rectus muscle.
   - If the globe were adducted 67°, the angle between the visual and orbital axes would be 90° (Fig. 16.4c). In this position the superior rectus could only act as an intortor.
2. **Inferior rectus** originates at the lower part of the annulus of Zinn and inserts 6.5 mm behind the inferior limbus.
   - The primary action of the inferior rectus is depression. Secondary actions are adduction and extorsion.
   - When the globe is abducted 23°, the inferior rectus acts purely as a depressor. As for superior rectus, this is the optimal position of the globe for testing the function of the inferior rectus muscle.
   - If the globe were adducted 67°, the inferior rectus could only act as an extortor.

Spiral of Tillaux

This is an imaginary line joining the insertions of the four recti and is an important anatomical landmark when performing surgery. The insertions get further away from the limbus and make a spiral pattern. The medial rectus insertion is closest (5.5 mm), followed by the inferior rectus (6.5 mm), lateral rectus (6.9 mm) and superior rectus (7.7 mm) (Fig. 16.5).

Oblique muscles

The obliques are inserted behind the equator and form an angle of 51° with the visual axis (*see* Fig. 16.2d).

1. **Superior oblique** originates superomedial to the optic foramen. It passes forwards through the trochlea at the angle between the superior and medial walls and is then

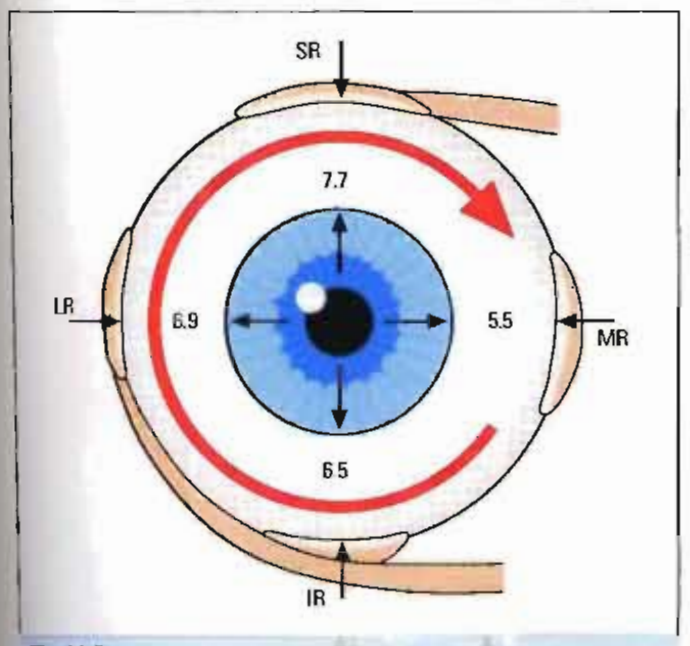

Fig. 16.5
Spiral of Tillaux (see *text*)

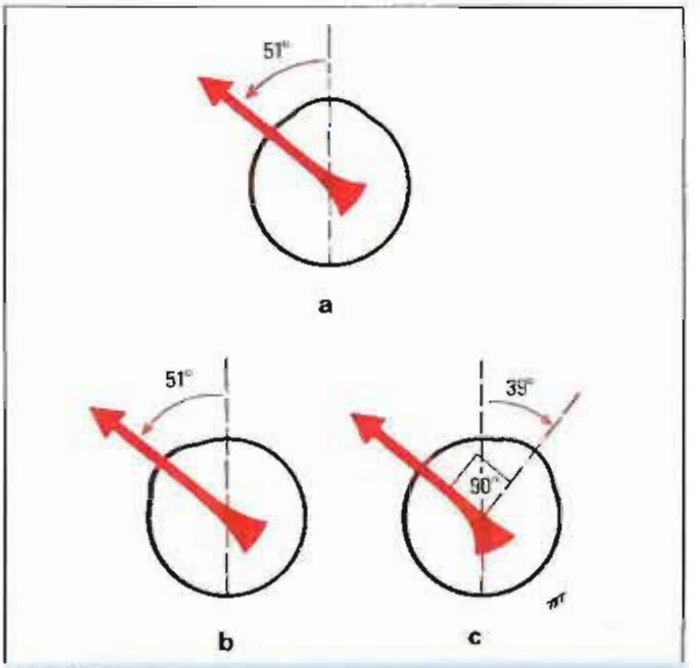

Fig. 16.6
Actions of the right superior oblique muscle (see *text*)

reflected backwards and laterally to insert in the posterior upper temporal quadrant of the globe.

- The primary action of the superior oblique is intorsion (Fig. 16.6a) Secondary actions are depression and abduction.
- When the globe is adducted 51°, the visual axis coincides with the line of pull of the muscle (Fig. 16.6b). In this position it can only act as a depressor. This is therefore the best position of the globe for testing the action of the superior oblique muscle.
- When the eye is abducted 39°, the visual axis and the superior oblique make an angle of 90° with each other (Fig. 16.6c). In this position the superior oblique can only cause intorsion.

2. **Inferior oblique** originates from a small depression just behind the orbital rim lateral to the lacrimal sac. It passes backwards and laterally, to insert in the posterior lower temporal quadrant of the globe, *close to the macula*.
   - The primary action of the inferior oblique is extorsion. Secondary actions are elevation and abduction.
   - When the globe is adducted 51°, the inferior oblique acts only as an elevator.
   - When the eye is abducted 39°, its main action is extorsion.

Nerve supply

1. **Lateral rectus** is supplied by the 6th cranial nerve (abducent nerve—abducting muscle).
2. **Superior oblique** is supplied by the 4th cranial nerve (trochlear nerve—muscle associated with the trochlea).
3. **Other muscles** and the levator muscle of the upper lid are supplied by the 3rd (oculomotor) nerve.

Ocular movements

Ductions

These are monocular movements around the axes of Fick. They consist of adduction, abduction, elevation, depression, intorsion and extorsion. They are tested by occluding the fellow eye and asking the patient to follow a target in each direction of gaze.

Versions

These are binocular, simultaneous, conjugate movements (in the same direction) (Fig. 16.7, top).

- Dextroversion and laevoversion (gaze right; gaze left), elevation (upgaze) and depression (downgaze). These four movements bring the globe into the *secondary* positions of gaze by rotation around either a horizontal (*X*) or a vertical (*Z*) axis of Fick.
- Dextroelevation and dextrodepression (gaze up and right; gaze down and right) and laevoelevation and laevodepression (gaze up and left; gaze down and left). These four oblique movements bring the eyes into the *tertiary* positions of gaze by rotation around both the horizontal and vertical axes.
- Dextrocycloversion and laevocycloversion (torsional movement of the superior limbi of both eyes to the right; torsion to the left).

Vergences

These are binocular, simultaneous, disjunctive movements (in opposite directions) (Fig. 16.7, bottom). Convergence is simul-

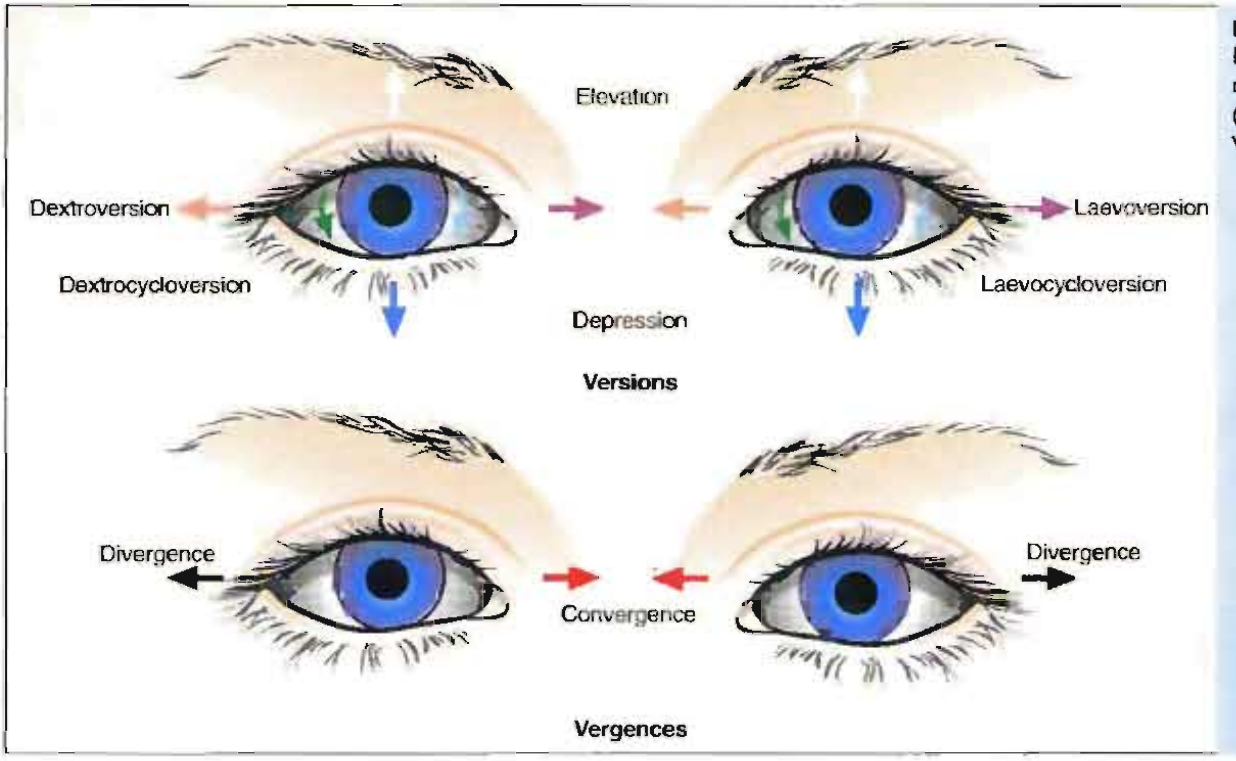

Fig. 16.7 Binocular movements (Courtesy of Wilmer Institute)

taneous adduction (inward turning); divergence is turning outwards from a convergent position. Convergence may be voluntary or reflex. Reflex convergence has four components:

1. **Tonic** convergence, which implies inherent innervational tone to the medial recti, when the patient is awake.
2. **Proximal** convergence is induced by psychological awareness of a near object.
3. **Fusional** convergence is an optomotor reflex, which maintains binocular single vision (BSV), by ensuring that similar images are projected onto corresponding retinal areas of each eye. It occurs without a change in refractive state of the eye and is initiated by bi-temporal retinal image disparity.
4. **Accommodative** convergence is induced by the act of accommodation as part of the synkinetic-near reflex. Each dioptre of accommodation is accompanied by a constant increment in accommodative convergence, giving the *'accommodative convergence by accommodation'* (AC/A) ratio. This is the amount of convergence in prism dioptres (Δ) per dioptre (D) change in accommodation. The normal value is 3–5 Δ. This means that 1 D of accommodation is associated with 3–5 Δ of accommodative convergence. It will be shown later that abnormalities of the AC/A ratio play an important role in the aetiology of strabismus.

Positions of gaze

1. **Six cardinal positions** of gaze are those in which one muscle in each eye has moved the eye into that position as follows:
   - Dextroversion (right lateral rectus and left medial rectus).
   - Laevoversion (left lateral rectus and right medial rectus).
   - Dextroelevation (right superior rectus and left inferior oblique).
   - Laevoelevation (left superior rectus and right inferior oblique).
   - Dextrodepression (right inferior rectus and left superior oblique).
   - Laevodepression (left inferior rectus and right superior oblique).
2. **Nine diagnostic positions of gaze** are those in which deviations are measured. They consist of the six cardinal positions, the primary position, elevation and depression (Fig. 16.8).

Laws of ocular motility

1. **Agonist–antagonist** pairs are muscles of the *same* eye that move the eye in *opposite* directions. The *agonist* is the primary muscle moving the eye in a given direction. The *antagonist* acts in the opposite direction to the agonist. For example, the right lateral rectus is the antagonist to the right medial rectus.
2. **Synergists** are muscles of the *same* eye that move the eye in the *same* direction. For example, the right superior rectus and right inferior oblique act synergistically in elevation.
3. **Yoke muscles** are *pairs of muscles*, one in each eye, that produce conjugate ocular movements. For example, the yoke muscle of the left superior oblique is the right inferior rectus.
4. **Sherrington law** of reciprocal innervation (inhibition) states that increased innervation to an extraocular muscle (e.g. right medial rectus) is accompanied by a reciprocal decrease in innervation to its antagonist (e.g. right lateral

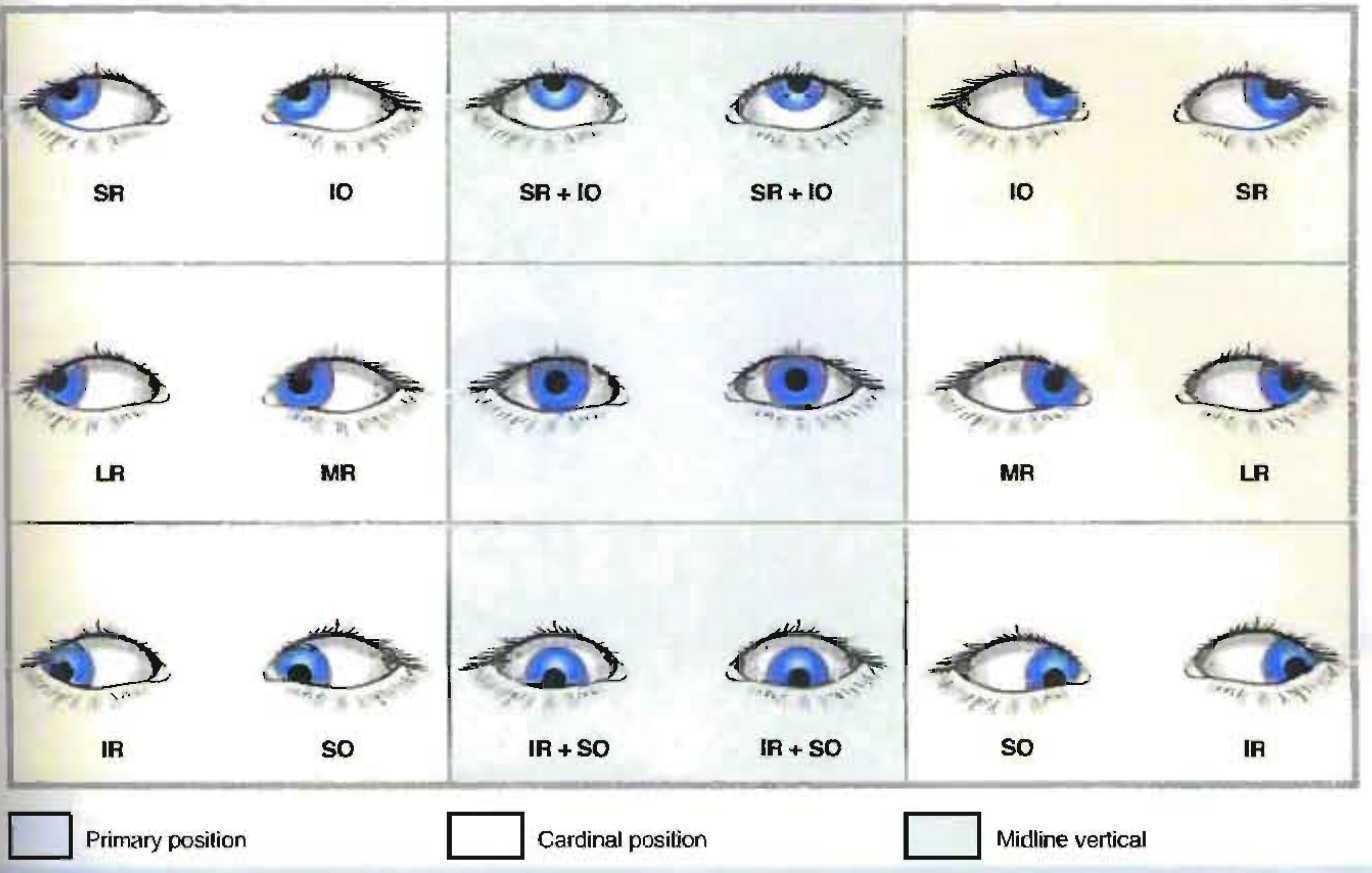

Fig. 16.8
Diagnostic positions of gaze (*see text*)

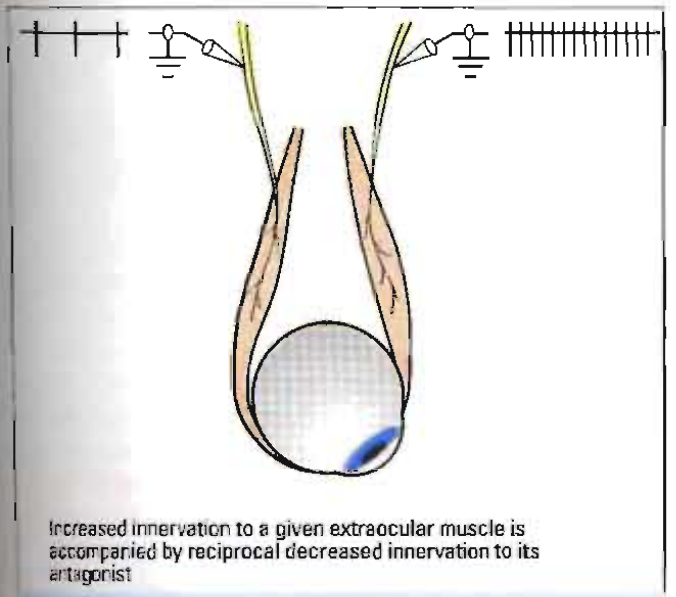

Fig. 16.9
Sherrington law of reciprocal innervation

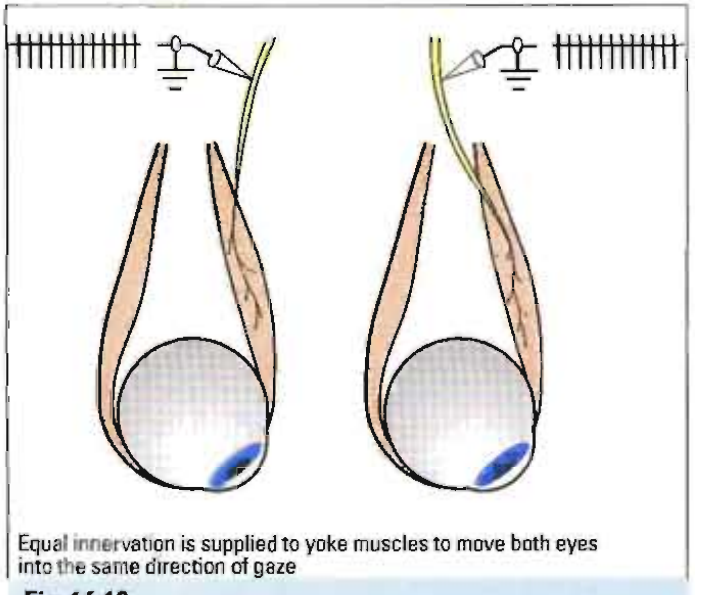

Fig. 16.10
Hering law of equal innervation of yoke muscles

rectus) (Fig. 16.9). This means that when the medial rectus contracts the lateral rectus automatically relaxes and vice versa. Sherrington law applies to both versions and vergences.

5. **Hering law** of equal innervation states that during any conjugate eye movement, equal and simultaneous innervation flows to the yoke muscles (Fig. 16.10). In the case of a paretic squint, the amount of innervation to both

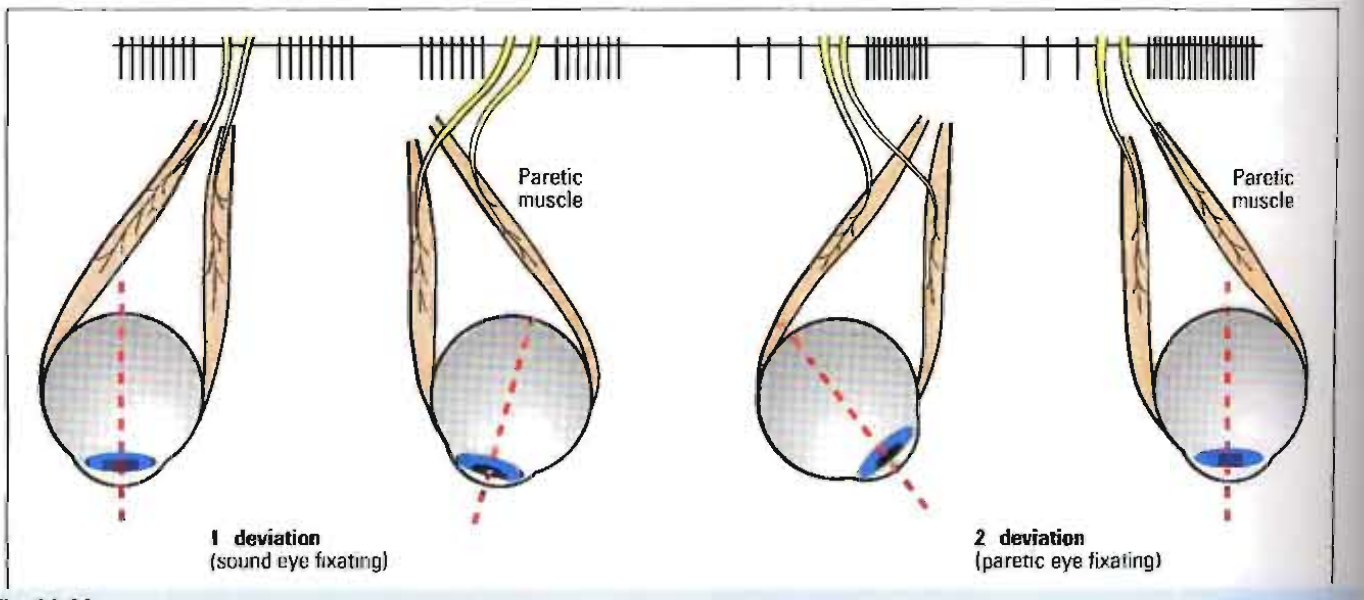

Fig. 16.11
Primary and secondary deviations in paretic strabismus (see *text*)

eyes is symmetrical, and always determined by the fixating eye, so that the angle of deviation will vary according to which eye is used for fixation. For example if, in the case of a left lateral rectus palsy, the right normal eye is used for fixation, there will be an inward deviation of the left eye due to the unopposed action of the antagonist of the paretic left lateral rectus (left medial rectus). The amount of misalignment of the two eyes in this situation is called the *primary deviation* (Figs 16.11, left and 16.12a). If the paretic left eye is now used for fixation, additional innervation will flow to the left lateral rectus, in order to establish this. However, according to Hering law, an equal amount of innervation will also flow to the right medial rectus (yoke muscle). This will result in an overaction of the right medial rectus and an excessive amount of adduction of the right eye. The amount of misalignment between the two eyes in this situation is called the *secondary deviation* (Figs 16.11, right and 16.12b). In a paretic squint, the secondary deviation exceeds the primary deviation.

Fig. 16.12
Left sixth nerve palsy. (a) Primary deviation; (b) secondary deviation (Courtesy of Wilmer Institute)

Functional consequences of strabismus

Amblyopia

Classification

Amblyopia is the unilateral, or (rarely) bilateral, decrease of best-corrected visual acuity caused by form vision deprivation and/or abnormal binocular interaction, for which there is no pathology of the eye or visual pathway.

1. **Strabismic** amblyopia results from abnormal binocular interaction where there is continued monocular suppression of the deviating eye. It is characterized by an impairment of vision which is present even when the eye is forced to fixate.
2. **Anisometropic** amblyopia is caused by a difference in refractive error of even as little as 1.0 D sphere. It results from abnormal binocular interaction from the superimposition of focused and unfocused images or from the superimposition of large and small images (aniseikonia). There may also be an element of form vision deprivation as one eye constantly receives a blurred image. It is frequently associated with microstrabismus and may coexist with strabismic amblyopia.

3. **Stimulus deprivation** amblyopia results from form vision deprivation. It may be unilateral or bilateral and is caused by opacities in the media (e.g. cataract) or severe ptosis.
4. **Iso-ametropic** amblyopia results from form vision deprivation. It is bilateral and is caused by high symmetrical refractive errors, usually hypermetropia.
5. **Meridional** amblyopia results from form vision deprivation in one meridian. It can be unilateral or bilateral and is caused by uncorrected astigmatism.

Diagnosis

1. **Visual acuity.** In the absence of an organic lesion, a difference in best corrected visual acuity of two lines or more is indicative of amblyopia. Visual acuity in amblyopia is often better while reading single letters than a row of letters. This 'crowding' phenomenon occurs to a certain extent in normal individuals but is more profound in amblyopes.
2. **Neutral density filter** is useful to differentiate impaired vision due to organic disease from amblyopia. A neutral density filter, which reduces visual acuity by two lines in a normal eye, is used as follows:
   a. Best corrected visual acuity is determined.
   b. The filter is placed in front of the eye and visual acuity measured
   c. No significant drop in visual acuity implies amblyopia.
   d. A significant drop in visual acuity implies an organic lesion.
3. **Grating acuity** (ability to perceive a grid pattern of different frequencies) often exceeds spatial (Snellen) acuity in amblyopia

NB: Visual fields and colour vision are normal.

Treatment

The sensitive period during which amblyopia can be reversed is up to 7–8 years in strabismic amblyopia and longer (up to 11–12 years) for anisometropic amblyopia.

1. **Occlusion** of the normal eye, to encourage use of the amblyopic eye, is the most effective treatment. The regimen, full-time or part-time, depends on the age of the patient and the density of amblyopia. The younger the patient, the more rapid the improvement, although the greater the risk of inducing amblyopia in the normal eye. It is therefore very important to monitor visual acuity in both eyes during treatment. The better the visual acuity at the start of occlusion, the shorter the duration required. If there has been no improvement after 6 months of occlusion, further treatment is unlikely to be fruitful.
2. **Penalization**, in which vision in the normal eye is blurred with atropine, is an alternative method. It may be used in the treatment of relatively mild amblyopia (6/24 or better) in association with hypermetropia. Penalization does not work as quickly as occlusion, and is only effective if vision in the normal eye is made worse that the vision in the amblyopic eye, at least for near.

NB: It is essential to exclude organic disease prior to commencing treatment for amblyopia.

Confusion and diplopia

Basic concepts

1. **Binocular single vision** (BSV) involves the simultaneous use of both eyes with bifoveal fixation, so that each eye contributes to a common single perception of the object of regard (Fig. 16.13a). Conditions necessary for BSV are:
   - Overlap of visual fields.
   - Accurate neuromuscular development and co-ordination, so that the visual axes are directed at the object.
   - Normal visual pathways.
   - Approximately equal image clarity and size in both eyes.
   - Corresponding retinal areas so that the eyes are cyclopean.
2. **Confusion** is the simultaneous appreciation of two superimposed but dissimilar images caused by stimulation of corresponding points (usually the foveae) by images of different objects (Fig. 16.13b).
3. **Diplopia** is the simultaneous appreciation of two images of the same object. It results from images of the same object falling on non-corresponding

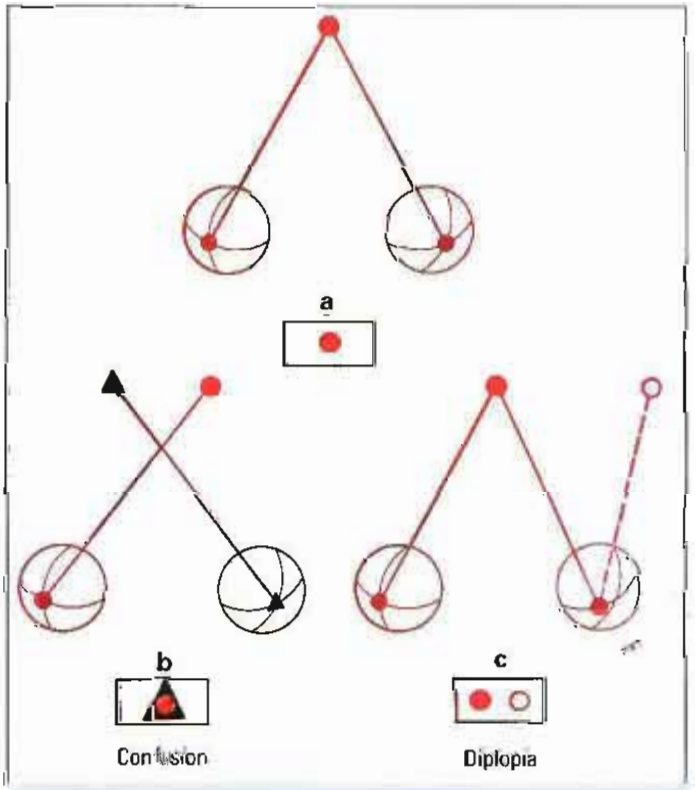

Fig. 16.13
Double vision (see text)

retinal points (Fig. 16.13c). Simultaneous (visual) perception is the ability to use both eyes simultaneously.

4. **Visual direction** is the projection of a given retinal element in a specific direction in subjective space.
   a. Principal visual direction is the direction in external space interpreted as the line of sight. This is normally the visual direction of the fovea.
   b. Secondary visual directions are the projecting directions of extrafoveal points with respect to the principal direction of the fovea.
5. **Projection** is the interpretation of the position of an object in space on the basis of stimulated retinal elements.
   - If a red object stimulates the right fovea (F), and a black object which lies in the nasal field stimulates a temporal retinal element (T), the red object will be interpreted by the brain as having originated from the straight ahead position and the black object will be interpreted as having originated in the nasal field (Fig. 16.14a). Similarly, nasal retinal elements project into the temporal field, upper retinal elements into the lower field and vice versa.
   - With both eyes open, the red fixation object is now stimulating both foveae, which are corresponding retinal points. The black object is now not only stimulating the temporal retinal elements in the right eye but also the nasal elements of the left eye. The right eye therefore projects the object into its nasal field and the left eye projects the object into its temporal field. However, because both of these retinal elements are corresponding points, they will both project the object into the same position in space (the left side) and there will be no double vision.
6. **Retino-motor values**. The image of an object in the peripheral visual field falls on an extrafoveal element. To establish fixation on this object a saccadic version of accurate amplitude is required. Each extrafoveal retinal element therefore has a retino-motor value proportional to its distance from the fovea, which guides the amplitude of saccadic movements required to 'look at it'. Retino-motor value, zero at the fovea, increases progressively towards the retinal periphery.
7. **Corresponding points** are areas on each retina that share the same subjective visual direction (for example, the foveae, which project straight ahead). Points on the nasal retina of one eye have corresponding points on the temporal retina of the other eye. This is the basis of normal retinal correspondence. For example, an object producing images on the right nasal retina and the left temporal retina will be projected into the right side of visual space.
8. **Horopter** is an imaginary plane in external space, all points on which stimulate corresponding retinal elements and are therefore seen singly (Fig. 16.14b). This plane passes through the intersection of the visual axes and therefore includes the point of fixation in BSV.
9. **Panum fusional area of BSV** is a zone in front of and behind the horopter in which objects (although not accurately stimulating corresponding retinal elements) are seen singly. Objects outside Panum area appear double. This is the basis of physiological diplopia. Panum area is narrow at fixation (6 seconds of arc) and broadens towards the periphery. Therefore objects on the horopter are seen singly. Objects in Panum fusional area are seen singly and stereoscopically. Objects outside Panum fusional area appear double.
10. **Sensory** fusion involves the integration, by the visual areas of the cerebral cortex, of two similar images, one from each eye, into one image. It may be central, which integrates images falling on the foveae, or peripheral, which integrates images falling outside the foveae.
11. **Motor** fusion involves the maintenance of physical alignment of the eyes to sustain bifoveal fixation. It is driven by retinal image disparity, which stimulates fusional vergences.
12. **Fusional vergence** involves disjunctive eye movements to overcome retinal image disparity. Fusional vergence amplitudes can be measured with prisms or on the synoptophore. Normal values are:
    - Convergence: about 15 Δ for distance and 25 Δ for near.

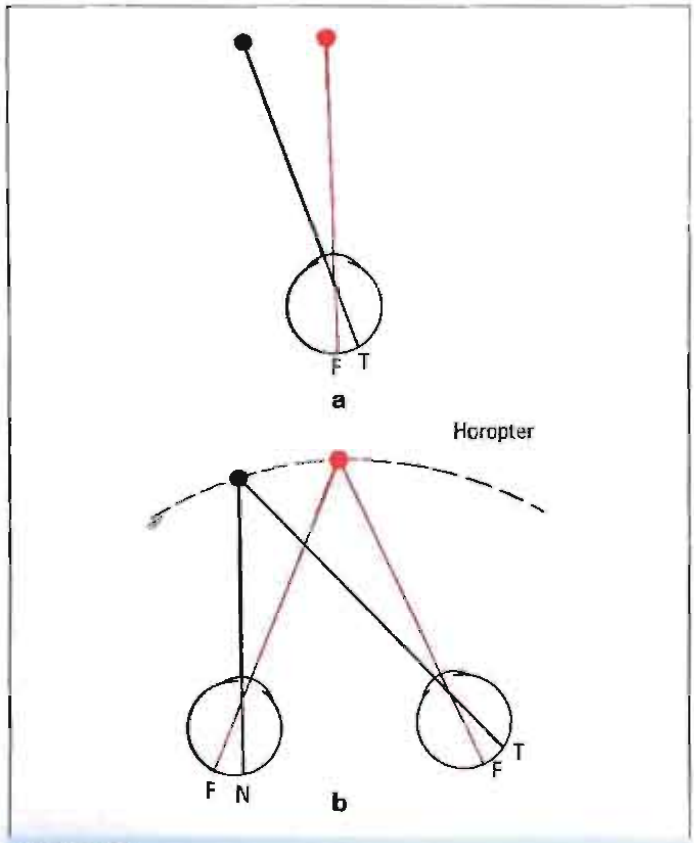

Fig. 16.14
Principles of projection (see text)

- Divergence: about 6 Δ for distance and 12 Δ for near.
- Vertical: 2–3 Δ.
- Cyclovergence: about 2–3°.

Fusional convergence helps to control an exophoria whereas fusional divergence helps to control an esophoria. The fusional vergence mechanism may be decreased by fatigue or illness, converting a phoria to a tropia. The amplitude of fusional vergence mechanisms can be improved by orthoptic exercises, particularly that of near fusional convergence for the relief of convergence insufficiency.

13. **Stereopsis** is the perception of depth (the third dimension, the first two being height and width). It arises when objects behind and in front of the point of fixation (but within Panum fusional area) stimulate horizontally disparate retinal elements simultaneously. The fusion of such disparate images results in a single visual impression perceived in depth. A solid object is seen stereoscopically (in 3D) because each eye sees a slightly different aspect of the object.

Sensory adaptation to strabismus

The ocular sensory system in children has the ability to adapt to anomalous states (confusion and diplopia) by two mechanisms: (a) *suppression* and (b) *abnormal retinal correspondence* (ARC). They occur because of the plasticity of the developing visual system in children under the age of 6–8 years. Rarely adults who develop sudden-onset strabismus are able to ignore the second image and therefore do not complain of diplopia.

1. **Suppression** involves active inhibition, by the visual cortex, of an image from one eye when *both eyes are open*. Stimuli for suppression include diplopia, confusion and a blurred image resulting from astigmatism/anisometropia. Clinically, suppression may be:
   a. ***Central*** or ***peripheral***. In central suppression the image from the fovea of the deviating eye is inhibited to avoid confusion. Diplopia, on the other hand, is eradicated by the process of peripheral suppression, in which the image from the peripheral retina of the deviating eye is inhibited.
   b. ***Monocular*** or ***alternating***. Suppression is monocular when the image from the dominant eye always predominates over the image from the deviating (or more ametropic) eye, so that the image from the latter is constantly suppressed. This type of suppression leads to the development of amblyopia. When suppression alternates (switches from one eye to the other), amblyopia does not develop.
   c. ***Facultative*** or ***obligatory***. Facultative suppression occurs only when the eyes are misaligned. Obligatory suppression is present at all times, irrespective of whether the eyes are deviated or straight.
2. **Abnormal retinal correspondence** (ARC) is a condition in which non-corresponding retinal elements acquire a common subjective visual direction. The fovea of the fixating eye is thus paired with a non-foveal element of the deviated eye. ARC is a positive sensory adaptation to strabismus (as opposed to suppression), which allows some binocular vision with limited fusion to be maintained in the presence of a heterotropia. ARC is most frequently present in small angle esotropia. It is rare in accommodative esotropia because of the variability of the angle of deviation, or in large angle deviations because the separation of the images is too great. It is also rarely found in exotropia because the deviation is often intermittent. When a child first develops strabismus, the following events occur:
   a. The fovea of the squinting eye is suppressed to avoid confusion.
   b. Diplopia will occur, since non-corresponding retinal elements receive the same image.
   c. To avoid diplopia, the patient will develop either peripheral suppression of the squinting eye or ARC.
   d. If suppression occurs this will subsequently lead to strabismic amblyopia.

> ***NB:*** The disadvantage of strongly entrenched ARC is that following surgery the patient may not revert to normal retinal correspondence. Therefore the angle of deviation may return to the pre-surgical state in an attempt to regain binocular vision.

Motor adaptation to strabismus

This involves the adoption of an abnormal head posture and occurs in adults who cannot suppress or in children with good binocular vision potential. Under strabismic conditions, patients will adopt an abnormal head posture to maintain BSV and eliminate diplopia. The patient will turn the head *into* the direction of the field of action of the weak muscle, so that the eyes are then automatically turned in the opposite direction and as far as possible *away* from its field of action (i.e. the head will turn where the eye cannot).

1. **Horizontal** deviation will result in a face turn. For example, if one of the muscles that turn the eyes to the left is paralysed, the face will also be turned to the left so that the eyes no longer need to look towards the left.
2. **Vertical** deviation will result in elevation or depression of the chin. If one of the elevators is weak, the chin will be elevated so that the eyes become depressed (Fig. 16.15).
3. **Torsional** deviation will result in a head tilt to one or the other shoulder. For example, if an intortor such as the left superior oblique is paralysed, the left eye will become extorted. In order to compensate for this, the head will tilt to the right shoulder, effectively 'intorting' the left eye (Fig. 16.16).

> ***NB:*** As a rule of thumb, a head tilt often accompanies vertical misalignments. The tilt is usually towards the lower eye, but not due to the vertical misalignment, but to the accompanying (and less apparent) torsional deviation.

Fig. 16.15
Compensatory chin elevation and head tilt

Fig. 16.16
Compensatory head tilt

Clinical evaluation

History

1. **Age of onset** can give an indication as to the aetiology of a squint. The earlier the onset, the more probable the need for surgical correction. The later the onset, the greater the likelihood of an accommodative component. Inspection of previous photographs may be useful for the documentation of strabismus or an abnormal head posture.
2. **Variability** is significant because intermittent strabismus indicates some degree of binocularity. An alternating deviation suggests symmetrical visual acuity in both eyes.
3. **General health** or developmental problems are significant: (e.g. children with cerebral palsy have an increased incidence of strabismus).
4. **Birth history**, including period of gestation, birth weight and any problems with delivery or in utero.
5. **Family history** is important because strabismus is frequently familial, although there is no definitive inheritance pattern. It is also important to know what therapy was necessary in other family members.

Visual acuity

Definition

Spatial visual acuity is the ability to distinguish separate elements of a target and identify it as a whole. It is quantified by the minimum angle of separation (subtended at the nodal point of the eye) between two objects that allows them to be perceived as separate. The normal minimum angle of separation is 1 minute or less, and corresponds to letters on the 6/6 line of the Snellen chart, when viewed from a distance of 6 metres.

Testing in preverbal children

An estimate of the comparative vision between the two eyes can be gained from simple examination and observation of the child.

1. **Occlusion of one eye**, if strongly objected to by the child, indicates poorer acuity in the other eye (Fig. 16.17).

Fig. 16.17
Amblyopic right eye. **(a)** No objection to occlusion of amblyopic eye; **(b)** objection to occlusion of normal eye
(Courtesy of Wilmer Institute)

2. **Fixation test** is performed as follows:
   a. A 16 Δ base-down prism is placed over one eye and the other is occluded.
   b. The eye behind the prism is therefore forced to elevate, to take up fixation.
   c. The eye behind the prism is then observed.
   d. Fixation is then graded as central or non-central and steady or unsteady.
   e. The other eye is uncovered and the ability to maintain fixation is observed.
   f. If fixation immediately returns to the uncovered eye, then visual acuity is impaired.
   g. If fixation is maintained through a blink, then visual acuity is good.
   h. If the patient alternates fixation, then the two eyes have equal vision.
   i. The test is repeated with the prism over the other eye.
   j. Monocular fixation should be central, steady and maintained in each eye.
3. '**Hundreds and thousands**' sweet test is a gross test which is seldom performed (Fig. 16.18). In principle, if the child is able to see and pick up small sweets at 33 cm, visual acuity is at least 6/24.
4. **Rotation test** is a gross qualitative test of the ability of an infant to fixate with both eyes open. The test is performed as follows:
   a. The examiner holds the child facing him and rotates briskly through 360°.
   b. If vision is normal, the eyes will deviate in the direction of rotation under the influence of the vestibulo-ocular response. The eyes intermittently flick back to the primary position to produce a rotational nystagmus.
   c. When rotation stops, the nystagmus should also cease due to suppression of post-rotatory nystagmus by fixation.
   d. If vision is severely impaired, the induced nystagmus does not stop when rotation ceases because the vestibulo-ocular response is not blocked by visual feedback.
5. **Preferential looking** tests can be used from early infancy. They are based on the fact that infants prefer to look at a pattern rather than a homogeneous stimulus. The infant is exposed to a stimulus and the examiner observes the eyes for fixation movements. Two examples are Teller acuity cards, which consist of black stripes of varying thickness, and Cardiff acuity cards, which consist of shapes with variable outlines (Fig. 16.19). Low-frequency (thick) gratings or shapes with a bold outline are seen more easily than those with thin outlines, and an assessment of visual acuity is made accordingly. Since grating acuity often exceeds Snellen acuity in amblyopia, Teller cards may overestimate visual acuity.
6. **Pattern visually evoked potential** gives a representation of spatial acuity but is more regularly used in the diagnosis of optic neuropathy.
7. **Optokinetic nystagmus** may provide an estimation of visual acuity dependent on the size of the stripes used.

Fig. 16.18
'Hundreds and thousands' test (see *text*)

In verbal children

1. **At age 2 years**, most children will have sufficient language skills to undertake a picture-naming test such as the Kay pictures (Fig. 16.20).
2. **At age 3 years**, most children will be able to undertake the matching of single-letter optotypes as in the Sheridan–Gardiner test (Fig. 16.21). This test has the disadvantage of overestimating acuity in the amblyopic eye as it eliminates the crowding phenomenon. The Keeler LogMAR crowded test (Fig. 16.22) is more accurate in amblyopia as it requires the child to match one letter out of a group of optotypes, which relates more accurately to Snellen acuity.
3. **At age 4 years**, most children will be able to perform a linear Snellen acuity test.

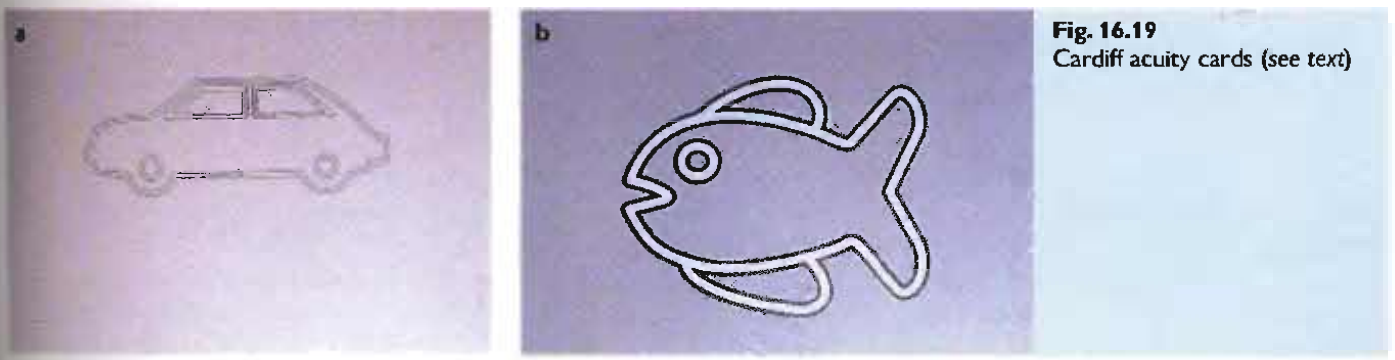

Fig. 16.19
Cardiff acuity cards (see *text*)

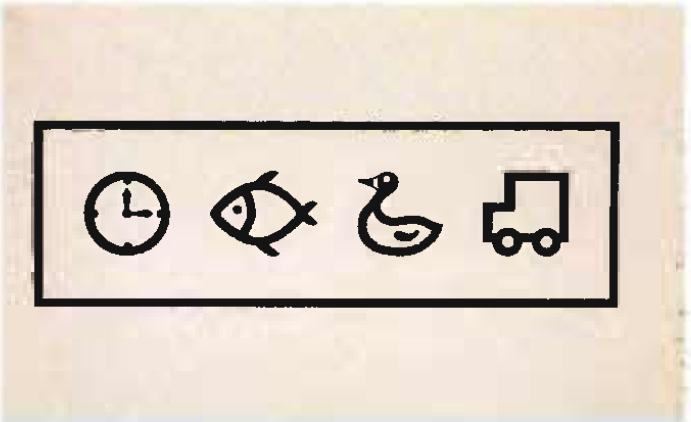

Fig. 16.20
Kay pictures (Courtesy of E. Dawson)

Fig. 16.21
Sheridan–Gardiner test (see text)

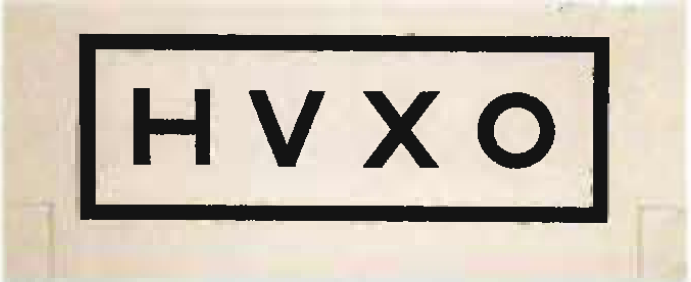

Fig. 16.22
Keeler LogMAR crowded test (see text) (Courtesy of E. Dawson)

Tests for stereopsis

Stereopsis is measured in seconds of arc (1° = 60 minutes of arc; 1 minute = 60 seconds of arc). It is useful to remember that normal spatial visual acuity is 1 minute and normal stereo-acuity is 60 seconds (which equals 1 minute). The lower the value, the better the acuity.

Fig. 16.23
Titmus test (see text)

Titmus

This test consists of a three-dimensional polaroid vectograph consisting of two plates in the form of a booklet which are viewed through polaroid spectacles. On the right is a large fly, and on the left are a series of circles and animals (Fig. 16.23). The test is performed at a distance of 16 inches (405 mm).

1. **Fly** is a test of gross stereopsis (3000 seconds of arc) and is especially useful for young children. The fly should appear 'solid' and the child is encouraged to pick up one of its wings. In the absence of gross stereopsis the fly will appear as an ordinary flat photograph. If the book is inverted, the targets will appear to recede. If the patient states that the fly's wings are still 'popping out', then they are not appreciating stereoscopic vision.
2. **Circles** comprise a graded series which tests fine depth perception. Each of the nine squares contains four circles. One of the circles in each square has a degree of disparity and will appear forward of the plane of reference in the presence of normal stereopsis. The angle of stereopsis is calculated from a chart provided with the test. The degree of disparity ranges from 800 to 40 seconds of arc. If a

patient perceives the circle to be shifted off to the side, then they are not appreciating stereoscopic vision, but are using monocular clues instead.

3. **Animals** is similar to the circles test but consists of three rows of animals, one of which will appear forward of the plane of reference. The degree of disparity ranges from 400 to 100 seconds of arc.

TNO

This random dot test consists of seven plates, which are viewed with red–green spectacles. Each plate contains various shapes (squares, crosses etc.) created by random dots in complementary colours. Some shapes are visible even without red–green spectacles (Fig. 16.24a) while others are 'hidden', and only apparent to an individual with stereopsis, while wearing red–green spectacles (Fig. 16.24b). The first three plates are used to establish the presence of stereoscopic vision and subsequent plates to quantify it. Because there are no monocular clues, the TNO test provides a truer measurement of stereopsis than the Titmus test. The degree of disparity ranges from 480 to 15 seconds of arc.

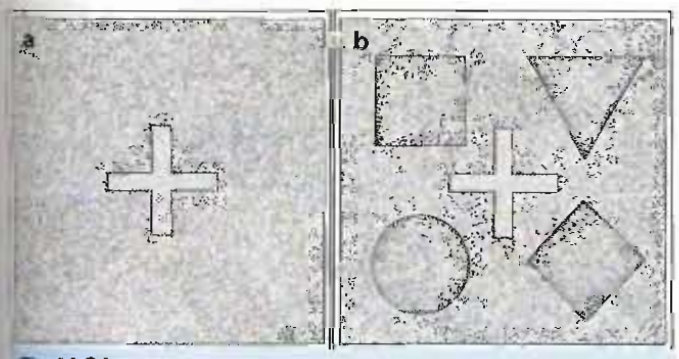

Fig. 16.24
TNO test (see *text*)

Lang

This test does not require special spectacles; the targets are seen alternately by each eye through the built-in cylindrical lens elements. Displacement of the dots creates disparity and the patient is asked to name or point to a simple shape, such as a star, on the card (Fig. 16.25). The Lang is especially useful in assessing stereopsis in very young children and babies, as they will instinctively reach out to touch the pictures. The examiner can also observe the child's eye movements from picture to picture on the card. The degree of disparity is quite gross, ranging from 1200 to 600 seconds of arc.

Frisby

This test consists of three transparent plastic plates of varying thickness. On the surface of each plate are printed four squares of small random shapes (Fig. 16.26). One of the squares contains a 'hidden' circle, in which the random shapes are printed on the reverse of the plate. The patient is required to identify this hidden circle. The test does not require special spectacles because the disparity is created by the thickness of the plate and can be varied by increasing or decreasing the working distance. The degree of disparity ranges from 600 to 15 seconds of arc.

Base-out prism

This is a quick and easy method for detecting BSV in children who cannot perform the stereo tests described above. The test is performed by placing a 20 Δ base-out prism in front of one eye (in this case the right). This displaces the retinal image temporally with resultant diplopia. The examiner observes corrective eye movements as follows:

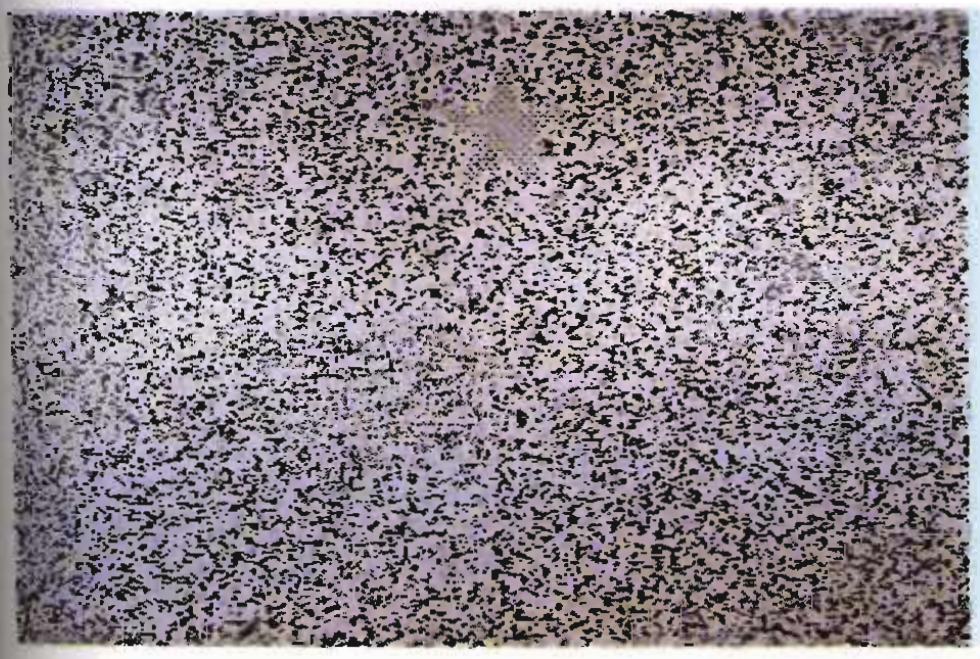

Fig. 16.25
Lang test (see *text*)

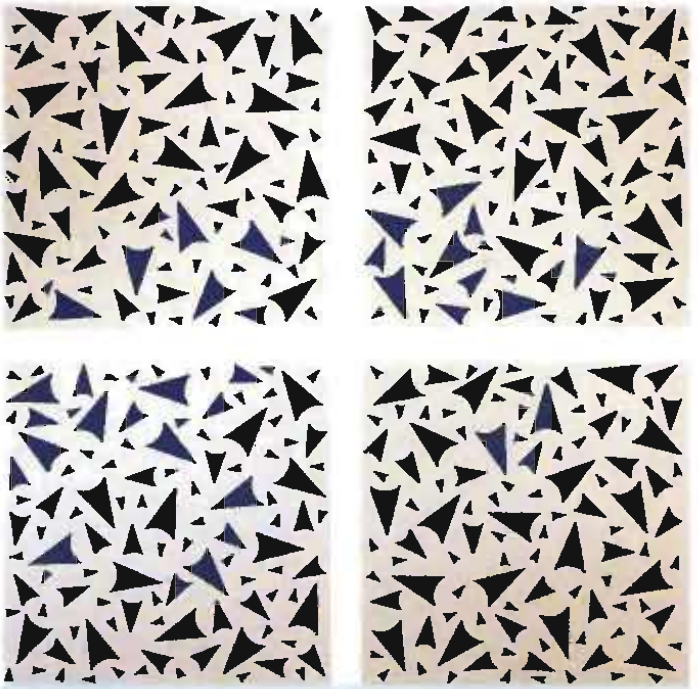

Fig. 16.26
Frisby test (see text)

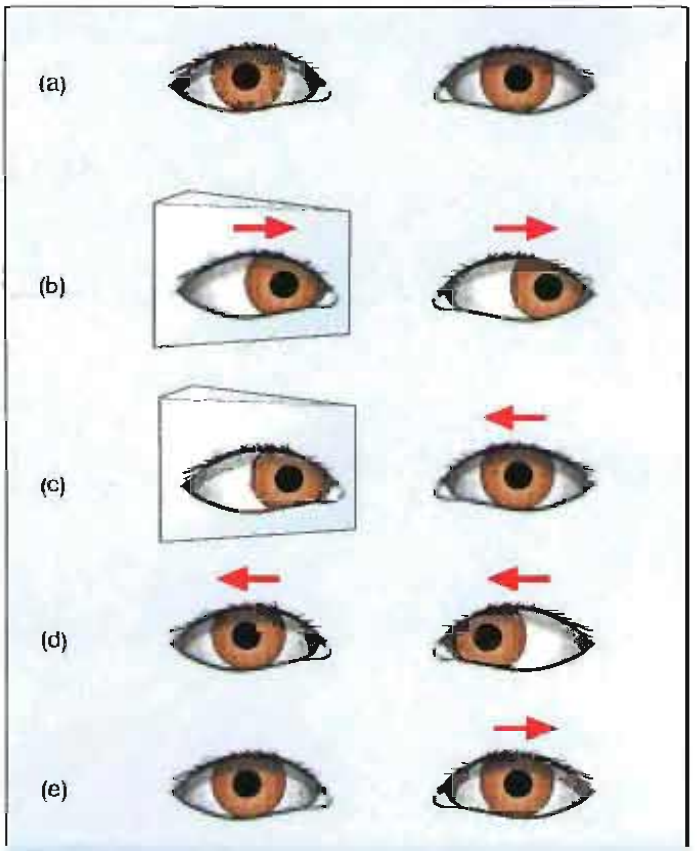

Fig. 16.27
Base-out prism test (see text)

a. There will be a shift of the right eye to the left to resume fixation (right adduction) with a corresponding shift of the left eye to the left (left abduction) in accordance with Hering law (Fig. 16.27b).

Fig. 16.28
Red–green goggles (Courtesy of Wilmer Institute)

b. The left eye will then make a corrective refixational saccade to the right (left re-adduction) (Fig. 16.27c).
c. On removal of the prism both eyes move to the right (Fig. 16.27d).
d. The left eye then makes an outward fusional movement (Fig. 16.27e).

> ***NB:*** Most children with good BSV should be able to overcome a 20 Δ prism; if not, weaker prisms (16 Δ or 12 Δ) may be tried.

Tests for sensory anomalies

Worth four-dot

1. Procedure
a. The patient wears a red lens in front of the right eye which filters out all colours except red.
b. A green lens is placed in front of the left eye, which will filter out all colours except green (Fig. 16.28).
c. The patient then views a box with four lights: one red, two green and one white.

2. Results (Fig. 16.29)
- If all four lights are seen, normal fusion is present.
- If all four lights are seen in the presence of a manifest deviation, ARC is present.
- If two red lights are seen, left suppression is present.
- If three green lights are seen, right suppression is present.
- If two red and three green lights are seen, diplopia is present.
- If the green and red lights alternate, alternating suppression is present.

Bagolini striated glasses

Each lens is covered with fine striations which convert a point source of light into a line, similar to the Maddox rod (see below).

1. Procedure
a. The two lenses are placed at 45° and 135° in front of each eye and the patient fixates a punctate light source (Fig. 16.30).

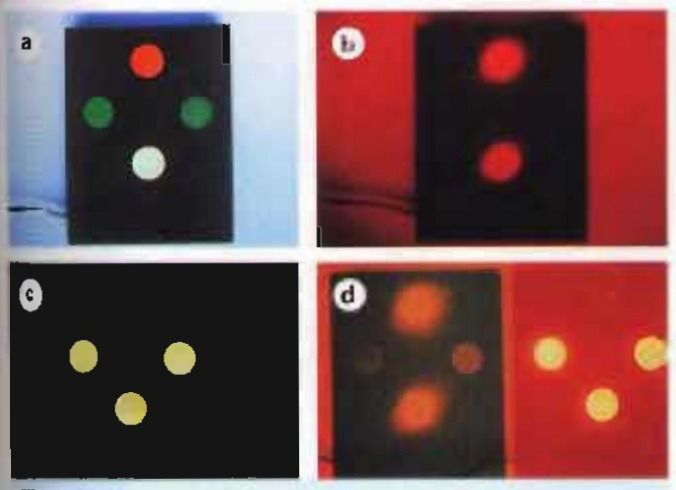

Fig. 16.29
Possible results of the Worth four-dot test (see text) (Courtesy of Wilmer Institute)

Fig. 16.31
Appearance of point of light through Bagolini lenses (Courtesy of Wilmer Institute)

Fig. 16.30
Bagolini test

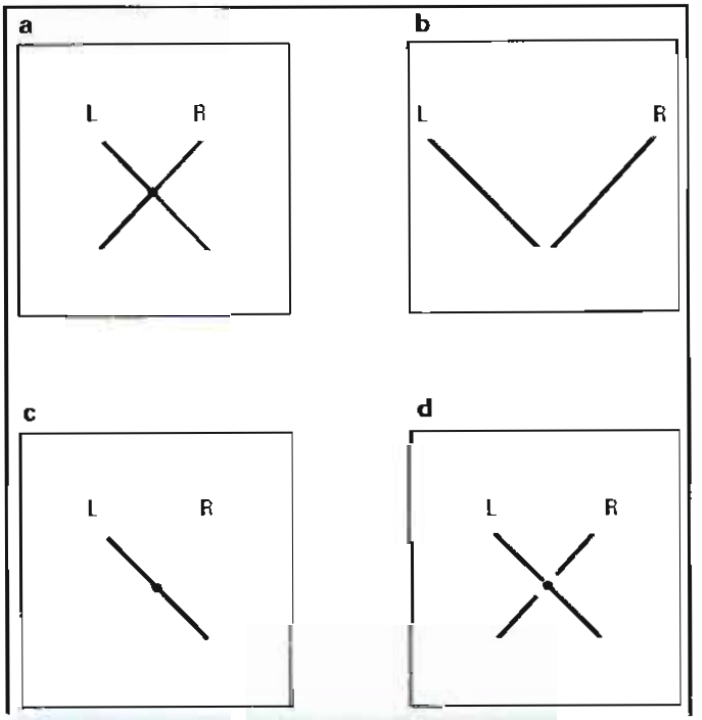

Fig. 16.32
Possible results of the Bagolini test (see text)

b. Each eye perceives an oblique line of light, perpendicular to that perceived by the fellow eye (Fig. 16.31).
c. Dissimilar images are thus presented to each eye under binocular viewing conditions.

2. **Results** cannot be interpreted correctly unless it is known whether or not strabismus is present:
   - If the two streaks intersect at their centres in the form of an oblique cross (an 'X'), the patient is either orthophoric or (if strabismic) has ARC (Fig. 16.32a).
   - If the two lines are seen but they do not form a cross, diplopia is present (Fig. 16.32b).
   - If only one streak is seen, there is no simultaneous perception (Fig. 16.32c).
   - If a small gap is seen in one of the streaks, a central suppression scotoma is present (Fig. 16.32d).

After-image

This test demonstrates the visual direction of the foveae.

1. **Procedure**
   a. One fovea is stimulated by a vertical bright flash of light and the fellow fovea is stimulated by a horizontal flash of light (Fig. 16.33).
   b. The vertical flash of light is harder to suppress and should therefore be applied to the deviating eye.
2. **Results**. The patient then draws the relative positions of the after-images.
   - If the two after-images are seen as a cross, retinal correspondence is normal (Fig. 16.34a).
   - If the two images do not cross, ARC is present.

Fig. 16.33
After-image test (Courtesy of Wilmer Eye Institute)

Fig. 16.35
Synoptophore

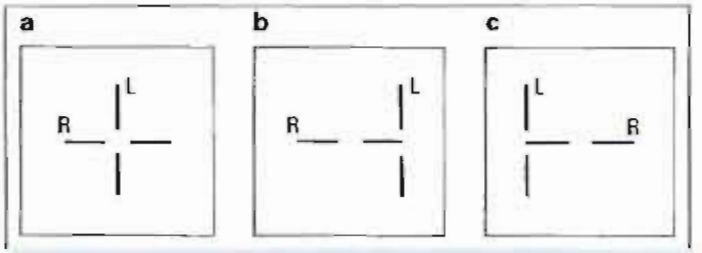

Fig. 16.34
Possible results of the after-image test (see *text*)

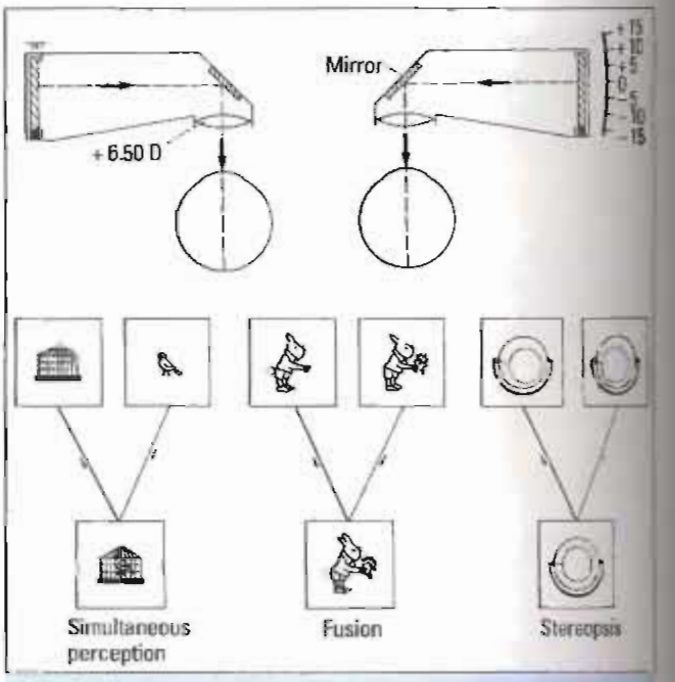

Fig. 16.36
Optical principles of the synoptophore (see *text*)

- In esotropia with ARC, the horizontal after-image (if presented to the right eye) is seen to the left of the vertical image (Fig. 16.34b).
- These findings are reversed in an exotropia (Fig. 16.34c).
- A patient with eccentric fixation will also see a cross. Eccentric fixation is a uniocular condition in which an extrafoveal part of the retina is used for fixation under both binocular and monocular conditions. There is a reorientation of the sensory and motor functions so that this new area usurps the principal visual direction once possessed by the fovea. The fovea of the dominant eye will perceive its after-image as straight ahead in visual space. With regard to the deviated eye, the eccentric area stimulated during the test will also perceive its after-image as straight ahead because that area has 'stolen' the principal visual direction.

Synoptophore

This is an instrument for assessing strabismus and quantifying binocular vision (Fig. 16.35). It can also detect suppression and ARC. The instrument consists of two cylindrical tubes with a mirrored right-angled bend and a +6.50 D lens in each eyepiece (Fig. 16.36, top). This optically sets the testing distance at about 6 metres. Pictures are inserted in a slide carrier situated at the outer end of each tube. The two tubes are supported on columns which enable the pictures to be moved in relation to each other, and any adjustments are indicated on a scale. The synoptophore can measure horizontal, vertical and torsional misalignments.

Grades of binocular vision

Binocular vision is graded on the synoptophore as follows (Fig. 16.36, bottom):

1. **First grade** (simultaneous perception) is tested by introducing two dissimilar but not mutually antagonistic pictures, such as a bird and a cage. The subject is then asked to put the bird into the cage by altering the columns. If the two pictures cannot be seen simultaneously, then either suppression or significant amblyopia is present. The

dissimilar objects are generally not seen in the same position in space. Retinal 'rivalry' will ensure that the image from one eye or the other predominates. However, here one picture is smaller than the other, so that while the small one is seen foveally, the larger one is seen parafoveally (and is thus placed in front of the deviating eye).

2. **Second grade** (fusion) is the ability of the two eyes to produce a composite picture from two similar pictures each of which is incomplete in one small different detail. The classic example is two rabbits, one lacking a tail and the other lacking a bunch of flowers. If fusion is present, one rabbit complete with tail and flowers will be seen. The range of fusion is then tested by moving the arms of the synoptophore so that the eyes have to converge and diverge in order to maintain fusion. It is obvious that the presence of simple fusion without any range is of little value in ordinary life.
3. **Third grade** (stereopsis) is the ability to obtain an impression of depth by the superimposition of two pictures of the same object which have been taken from slightly different angles. The classic example is the bucket which is appreciated in three dimensions.

Detection of ARC

ARC can be detected on the synoptophore as follows:

1. The examiner determines the objective angle of the deviation by presenting each fovea alternately with a target until no movement of the eyes is seen.
2. If the images are seen superimposed with the angle between the arms of the synoptophore equal to the objective angle of squint, then retinal correspondence is normal.
3. If the objective and subjective angles are different, ARC is present. The difference in degrees between the subjective and objective angles is the angle of anomaly. ARC is said to be harmonious when the objective angle equals the angle of anomaly and unharmonious when it exceeds the angle of anomaly. In harmonious ARC the subjective angle is zero (i.e. theoretically there will be no movement on a cover test).

Measurement of deviation

Hirschberg test

This gives a rough objective estimate of the angle of a manifest strabismus in uncooperative patients or when fixation is poor. A pen-torch is shone into the eyes from arm's length and the patient is asked to fixate the light. The corneal reflection of the light will be (more or less) centred in the pupil of the fixating eye, but will be decentred in a squinting eye, in the direction opposite to that of the deviation. The distance of the corneal light reflection from the centre of the pupil is noted. The premise is that every millimetre of deviation is equal to 7° (15 Δ). For example, if the reflex is situated at the temporal border of the pupil (assuming a pupillary diameter of 4 mm), the angle is about 30 Δ (Fig. 16.37); if it is at the limbus, the angle is about 90 Δ

Fig. 16.37
Hirschberg test. The right corneal reflex is near the temporal border of the pupil indicating an angle of about 30 Δ (15°)

Fig. 16.38
Hirschberg test. The left corneal reflex is at the limbus indicating an angle of about 90 Δ (45°)

(Fig. 16.38). This test is also useful in detecting pseudostrabismus, which may be caused by the following conditions:

1. **Pseudo-esotropia**
   - *a. Epicanthic folds* (*see* Fig. 1.138).
   - *b. Short interpupillary distance* due to close-set eyes.
   - *c. Negative angle kappa*. Angle kappa is the angle between the visual and anatomical axes (Fig. 16.39b). Normally, the fovea is situated temporal to the posterior pole. The eyes are therefore slightly abducted to achieve bifoveal fixation. A light shone onto the cornea will therefore cause a reflex just nasal to the centre of the cornea in both eyes. This is termed a positive angle kappa: if large it may simulate an exotropia (Fig. 16.39a). A negative angle kappa occurs when the fovea is situated nasal to the posterior pole (high myopia and ectopic fovea). In this situation, the corneal reflex is situated temporal to the centre of the cornea and it may simulate an esotropia.
2. **Pseudo-exotropia**
   - *a. Wide interpupillary distance* (Fig. 16.40).
   - *b. Positive angle kappa*, as described above.

Krimsky test

In this test, prisms are placed in front of the fixating eye until the corneal light reflexes are symmetrical (Fig. 16.41). It is important to note that a Krimsky test does not dissociate the eyes and only measures a manifest deviation. Since it does not

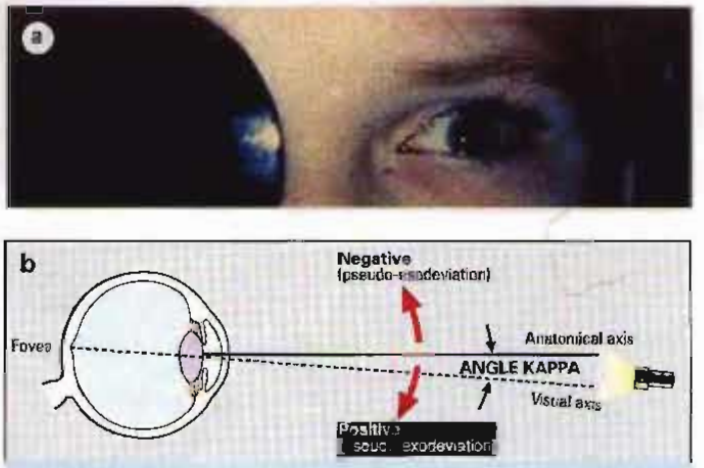

Fig. 16.39
Angle kappa (see *text*) (Courtesy of Wilmer Institute)

Fig. 16.42
Cover test (see *text*)

Fig. 16.40
Pseudo-exotropia due to a wide interpupillary distance

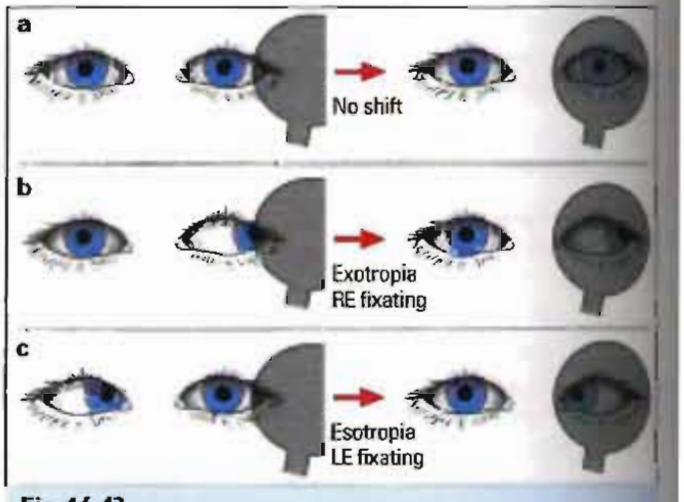

Fig. 16.43
Possible results of the cover test (see *text*)

Fig. 16.41
Krimsky test (Courtesy of K. Nischal)

take into account any latent component, it often underestimates the true size of the deviation.

Cover tests

By far the most accurate assessment of a deviation is with the cover tests. These tests allow the examiner to differentiate tropias from phorias, assess the degree of control of a deviation, and note fixation preference and strength of fixation for each eye. These tests are based on the patient's ability to fixate. Attention and cooperation are also required.

1. **Cover–uncover test** consists of two parts:
   a. *Cover test* to detect a heterotropia. It should be performed both for near (using an accommodative target) (Fig. 16.42) and for distance as follows:
      - The patient fixates a straight-ahead target.
      - If a right deviation is suspected, the examiner covers the opposite left eye and notes any movement of the right eye.
      - No shift indicates either orthophoria (Fig. 16.43a) or left heterotropia (Fig. 16.43b).
      - Adduction of the right eye to take up fixation indicates exotropia and abduction, esotropia (Fig. 16.43c).
      - Downward movement indicates hypertropia and

upward movement, hypotropia.
- The test is repeated on the opposite eye.

b. Uncover test to detect a heterophoria. It should be performed both for near (using an accommodative target) and for distance as follows:
- The patient fixates a straight-ahead distant target.
- The examiner covers the right eye and after a few seconds removes the cover (Fig. 16.44).
- No movement indicates orthophoria (Fig. 16.45a), although a keen observer will frequently detect a very slight latent deviation in most normal individuals, as very few people are truly orthophoric.
- If the right eye had deviated while under cover, it will manifest a re-fixation movement on being uncovered.
- Adduction of the right eye indicates exophoria (Fig. 16.45b) and abduction, esophoria (Fig. 16.45c).
- Upward or downward movement indicates a vertical phoria. In the context of latent strabismus, it is never certain whether one eye is 'hypo' or the other eye 'hyper', unlike with a manifest squint.

Fig. 16.44
Uncover test (see *text*) (Courtesy of Wilmer Institute)

- The test is repeated for the opposite eye.

> ***NB:*** Most examiners perform the cover test and the uncover test simultaneously, hence the term cover–uncover test.

2. **Alternate cover test** interrupts binocular fusion mechanisms and reveals the total deviation (phoria plus tropia) (Fig. 16.46). It should be performed after the cover–uncover test because if performed first it will be impossible to differentiate phoria from tropia.
   a. The right eye is covered for about 2 seconds.
   b. The occluder is quickly shifted to the opposite eye for 2 seconds, then back and forth several times.
   c. After the cover is removed, the examiner notes the speed and smoothness of recovery as the eyes return to their pre-dissociated state.
   d. A patient with a heterophoria will have straight eyes before and after the test has been performed (Fig. 16.46a), whereas a patient with a heterotropia will have a manifest deviation (Fig. 16.46b and c).
3. **Prism cover test** precisely measures the angle of deviation. It is performed as follows:
   a. The alternate cover test is first performed.
   b. Prisms of increasing strength are placed in front of one eye with the base opposite the direction of the deviation (i.e. point the apex of the prism in the direction of the deviation). For example, in a convergent strabismus the prism is held base-out.
   c. The alternate cover test is continuously performed (Fig. 16.47). As stronger prisms are brought in, the amplitude of ocular re-fixation movements gradually decreases.
   d. The end-point is reached when ocular movements are negated; the angle of deviation then equals the strength of the prism.

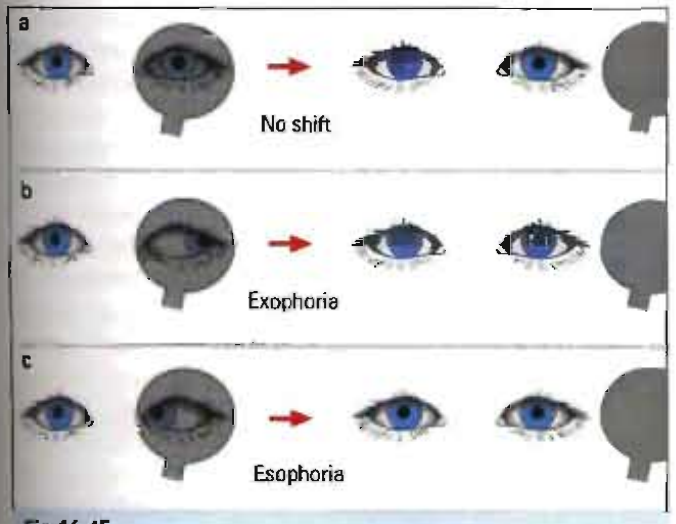

Fig. 16.45
Possible results of the uncover test (see *text*)

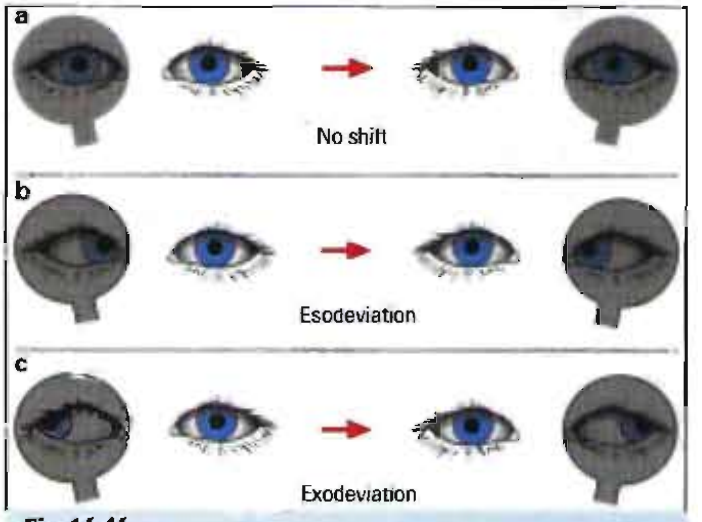

Fig. 16.46
Possible results of the alternate cover test (see *text*)

Fig. 16.47
Prism cover test (see text)

Fig. 16.49
Maddox rod test (see text) (Courtesy of Wilmer Institute)

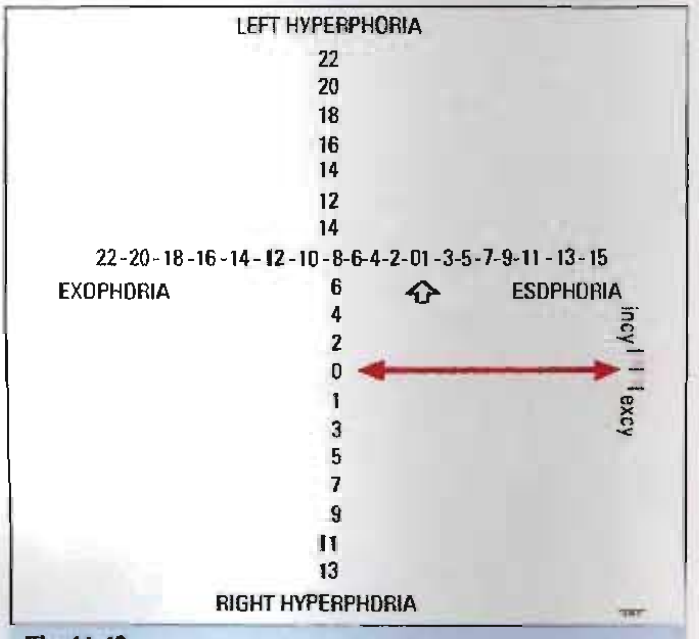

Fig. 16.48
Maddox wing (see text)

Fig. 16.50
Appearance of a point of light through Maddox rods (Courtesy of Wilmer Institute)

Dissimilar image tests

1. **Maddox wing** dissociates the eyes for near fixation (1/3 m) and measures heterophoria. The instrument is constructed in such a way that the right eye sees only a white vertical arrow and a red horizontal arrow, whereas the left eye sees only horizontal and vertical rows of numbers (Fig. 16.48). Measurements are made as follows:
   - The horizontal deviation is measured by asking the patient to which number the white arrow points.
   - The vertical deviation is measured by asking the patient which number the red arrow intersects.
   - The amount of cyclophoria is determined by asking the patient to move the red arrow so that it is parallel with the horizontal row of numbers.

2. **Maddox rod** consists of a series of fused cylindrical red glass rods (Fig. 16.49) which convert the appearance of a white spot of light into a red streak (Fig. 16.50). The optical properties of the rods cause the streak of light to be at an angle of 90° to the long axis of the rods; when the glass rods are held horizontally, the streak will be vertical and vice versa. The test is performed as follows:
   - The rod is placed in front of the right eye. This dissociates the two eyes because the red streak seen by the right eye cannot be fused with the unaltered white spot of light seen by the left eye (Fig. 16.51).
   - The amount of dissociation is measured by the superimposition of the two images using prisms. The base of the prism is placed in the position opposite to the direction of the deviation.
   - Both vertical and horizontal deviations can be measured in this way but the test cannot differentiate phoria from tropia.

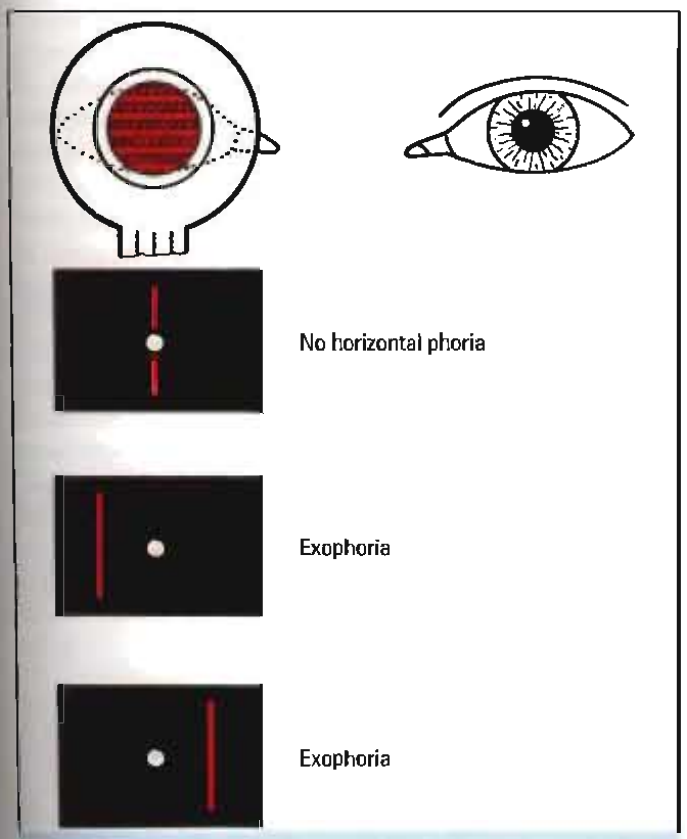

Fig. 16.51
Possible results of the Maddox rod test (see *text*)

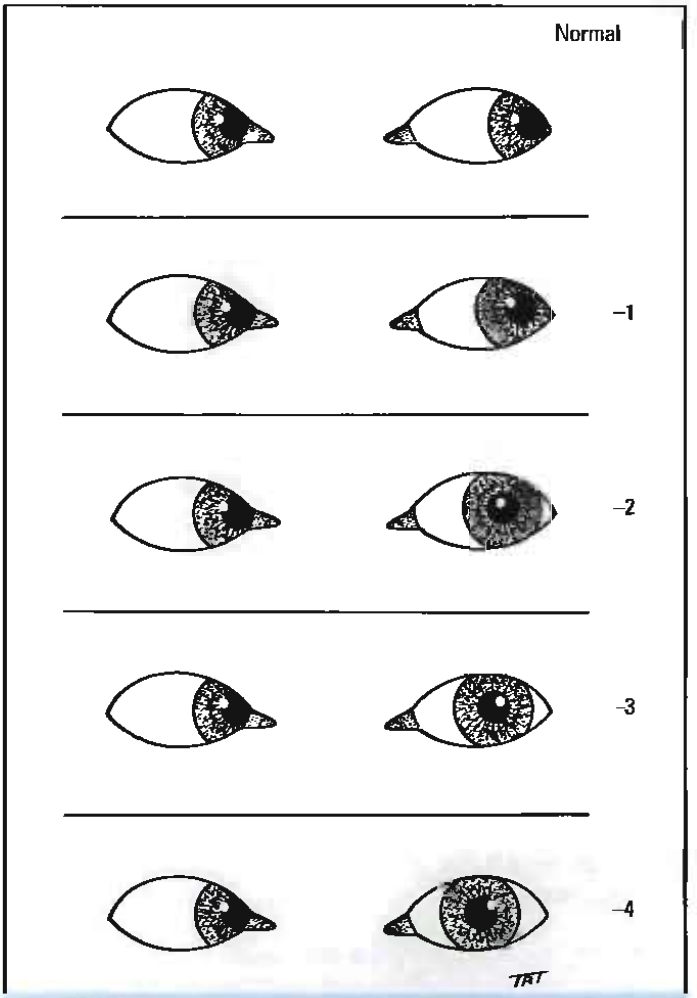

Fig. 16.52
Grading of left lateral rectus underaction

Motility tests

Ocular movements

Examination of ocular movements involves assessment of smooth pursuit movements followed by that of saccadic movements.

1. **Versions** towards the eight eccentric positions of gaze are tested by asking the patient to follow a target, usually a pen or pen-torch (which offers the advantage of corneal light reflections to aid assessment). They may also be elicited voluntarily, acoustically or by the doll's head manoeuvre.
2. **Ductions** are assessed if reduced ocular motility is noted in either or both eyes. A pen-torch should be used with careful attention to the position of the corneal reflexes. The fellow eye is occluded and the patient asked to follow the torch into various positions of gaze. A simple numeric system may be employed using 0 to denote full movement, and –1 to –4 to denote increasing degrees of underaction (Fig. 16.52).

Fig. 16.53
RAF rule (see *text*) (Courtesy of Wilmer Institute)

Near point of convergence

The near point of convergence (NPC) is the nearest point on which the eyes can maintain fixation. It can be measured with the RAF rule, which rests on the patient's cheeks (Fig. 16.53). A target is slowly moved along the rule towards the patient's eyes until one eye loses fixation and drifts laterally (objective NPC). The subjective NPC is the point at which the patient reports diplopia. Normal NPC should be nearer than 10 cm.

Near point of accommodation

The near point of accommodation (NPA) is the nearest point on which the eyes can maintain clear focus. It can also be measured with the RAF rule. The patient fixates a line of print, which is then slowly moved towards the patient until it becomes blurred. The distance at which this is first reported is read off the rule and denotes the NPA. The NPA recedes with the age: when sufficiently far away to render reading difficult without optical correction, this indicates presbyopia. At the age of 20 years the NPA is 8 cm and by the age of 50 years it has receded to 46 cm.

Fusional amplitudes

These measure the efficacy of disjunctive movements. They may be tested with prisms or the synoptophore. Increasingly strong prisms are placed in front of one eye, which will then abduct or adduct (depending on whether the prism is base-in or base-out respectively), in order to maintain bifoveal fixation. When a prism greater than the fusional amplitude is reached, diplopia is reported or one eye drifts the other way. This is the limit of vergence ability.

NB: The prism fusion range must be assessed in any patient where there is a risk of diplopia developing after strabismus surgery.

Refraction and fundoscopy

It should be emphasized that dilated fundoscopy is *mandatory* in the context of strabismus, to exclude any underlying ocular pathology such as macular scarring, optic disc hypoplasia or retinoblastoma. Strabismus is often secondary to refractive error. Hypermetropia, astigmatism, anisometropia and myopia may all be associated with strabismus.

Cycloplegia

The commonest refractive error causing strabismus is hypermetropia. Accurate measurement of hypermetropia necessitates effective paralysis of the ciliary muscle (cycloplegia), in order to neutralize the effect of accommodation, which masks the true degree of this refractive error.

1. **Cyclopentolate** affords adequate cycloplegia in most children. The concentration employed is 0.5% under the age of 6 months and 1% thereafter. One drop, repeated after 5 minutes, usually results in maximal cycloplegia within 30 minutes, with recovery of accommodation after 24 hours. The adequacy of cycloplegia can be determined by comparing retinoscopy readings with the patient fixating for distance and then for near. If cycloplegia is adequate, there will be little or no difference. If cycloplegia is incomplete there will be a difference between the two readings and it may be necessary to wait another 15 minutes or to instil another drop.

NB: Topical anaesthesia with an agent such as proxymetacaine, prior to instillation of cyclopentalate, is useful in preventing ocular irritation and reflex tearing, thus affording better retention of the cyclopentolate in the conjunctival sac and effective cycloplegia.

2. **Atropine** may be necessary in some children under the age of 4 years with either high hypermetropia or heavily pigmented irides, in whom cyclopentolate may be inadequate. Atropine may be used as drops or ointment, although drops are easier for an untrained person to instil. The concentration is 0.5% under the age of 12 months and 1% thereafter. Maximal cycloplegia occurs at 3 hours, recovery of accommodation starts after about 3 days and is usually complete by 10 days. Atropine is instilled (by the parents) t.i.d. for 3 days before retinoscopy. The parents should be warned to discontinue medication if there are signs of systemic toxicity, such as flushing, fever or restlessness, and seek immediate medical attention.

When to prescribe?

Any significant refractive error should be corrected, particularly in patients with anisohypermetropia or anisoastigmatism associated with amblyopia.

1. **Hypermetropia.** The lowest hypermetropic correction worth prescribing depends on the age and ocular alignment. In the absence of esotropia in a child under the age of 2 years this is +4.00 D, although in an older child it is worth prescribing +2.00 D. However, in the presence of esotropia a correction of +2.00 D should be prescribed, even under the age of 2 years.
2. **Astigmatism.** A cylinder of 1.00 D or more should be prescribed, especially in cases of anisometropia.
3. **Myopia.** The necessity for correction depends on the age of the child. Under the age of 2 years, −5.00 D or more of myopia should be corrected; between the ages of 2 and 4 the amount is −3.00 D. Older children should have correction of even milder degrees of myopia to allow clear distance vision.

Change of refraction

Because refraction changes with age, it is important to check every 6 months. At birth most babies are hypermetropic. After the age of 2 years there may be an increase in hypermetropia and a decrease in astigmatism. Hypermetropia may continue to increase until the age of about 6 years, and then between the ages of 6 and 8 years levels off, subsequently decreasing until the early teenage years. Children under the age of 6 years, with less than +2.50 D, are often virtually emmetropic by the age of 14 years. However, an esotrope under the age of 6 years, with more than +4.00 D, is unlikely to lose sufficient hypermetropia to maintain straight eyes without spectacles.

Investigation of diplopia

The Hess test and the Lees screen plot ocular position as a function of the extraocular muscles and enable differentiation of paretic strabismus caused by neurological pathology from restrictive myopathy such as in thyroid eye disease or a blow-out fracture of the orbit.

Hess test

The screen contains a tangent pattern printed onto a dark-grey background. Red lights that can be individually illuminated indicate the positions of gaze of each of the extraocular muscles.

1. The patient is seated 50 cm from the screen and wears red–green goggles, red lens in front of the right eye, and holds a green 'laser' pointer.
2. The examiner projects a vertical slit of red light onto the screen from a red 'laser' pointer, which is used as the point of fixation. This can now be seen only with the right eye, which therefore becomes the fixating eye.
3. The patient is asked to superimpose their horizontal slit of green light onto the red light.
4. In orthophoria the two lights should be more or less superimposed in all nine positions of gaze.
5. The goggles are then reversed (red filter in front of the left eye) and the procedure is repeated.
6. The relative positions are connected with straight lines.

Lees screen

The apparatus consists of two opalescent glass screens at right-angles to each other, bisected by a two-sided plane mirror which dissociates the two eyes (Fig. 16.54). Each screen has a tangent pattern marked onto the back surface which is revealed only when the screen is illuminated. The test is performed with each eye fixating in turn.

Fig. 16.54
Lees screen (see text)

1. The patient faces the non-illuminated screen and fixates the dots in the mirror.
2. The examiner indicates the dot required for the patient to plot.
3. The patient positions the pointer on the non-illuminated screen perceived to be on top of the dot indicated by the examiner.
4. When all of the dots have been plotted the patient is repositioned to face the other screen and the procedure is repeated.

Interpretation

1. The two charts are compared (Fig. 16.55).
2. The smaller chart indicates the eye with the paretic muscle (right eye).
3. The larger chart indicates the eye with the overacting muscle (left eye).
4. The smaller chart will show its greatest restriction in the main direction of action of the paretic muscle (right lateral rectus).
5. The larger chart will show its greatest expansion in the main direction of action of the yoke muscle (left medial rectus).

Changes with time

Changes with time are also extremely useful as a prognostic guide. For example, in right superior rectus palsy, the Hess chart will show underaction of the affected muscle with an overaction of its yoke muscle (left inferior oblique) (Fig. 16.56a). Because of the great incomitance of the two charts, the diagnosis is straightforward. If the paretic muscle recovers its function, both charts will revert to normal. However, if the paresis persists, the shapes of both charts will change as follows:

- Secondary contracture of the ipsilateral antagonist (right inferior rectus) will show up on the chart as an overaction which will lead to a secondary (inhibitional) palsy of the antagonist of the yoke muscle (left superior oblique), which will show up on the chart as an underaction (Fig. 16.56b). This could lead to the incorrect impression that the left superior oblique was the primary muscle at fault.

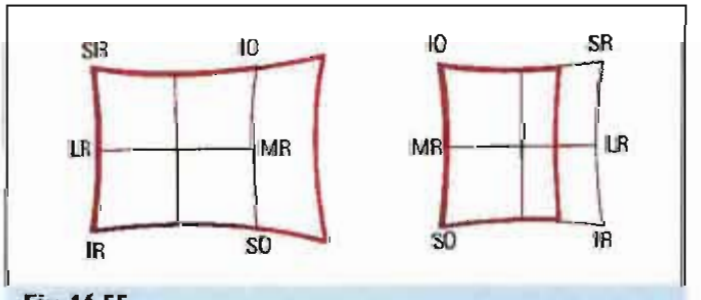

Fig. 16.55
Hess chart of a recent right lateral rectus palsy (see text)

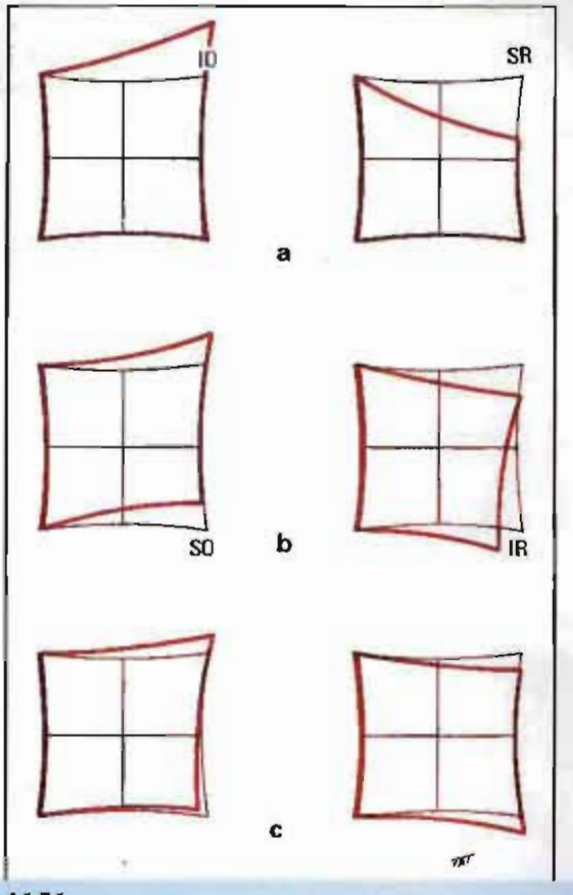

Fig. 16.56
Hess chart showing changes with time of a right superior rectus palsy (see text)

- With further passage of time, the two charts become more and more concomitant until it may be impossible to determine which was the primary paretic muscle (Fig. 15.56c).

Clinical examples

It is worth analysing the following examples after gaining a knowledge of ocular motor nerve palsies from Chapter 18.

1. **Left third nerve palsy** shows the following (Fig. 16.57):
   - Contraction of the left chart and expansion of the right.
   - Left exotropia: note that the fixation spots in the inner charts of both eyes are deviated laterally. The deviation is more on the right chart (when the left eye is fixating), indicating that secondary deviation exceeds the primary, as is typical of a paretic squint.
   - Left chart shows underaction of all muscles except the lateral rectus and superior oblique.
   - Right chart shows overactions of all muscles except the medial rectus and inferior rectus, the 'yokes' of the spared muscles.
2. **Right fourth nerve palsy** shows the following (Fig. 16.58):
   - No significant differences in chart size.
   - Right hypertropia: note that the fixation spot of the right inner chart is deviated upwards and the left is deviated downwards. The chart also illustrates that this hypertropia increases on laevoversion, and disappears on dextroversion.
   - Right chart shows underaction of the superior oblique and overaction of the inferior oblique.
   - Left chart shows overaction of the inferior rectus and underaction (inhibitory palsy) of the superior rectus.
3. **Right sixth nerve palsy** shows the following (Fig. 16.59):
   - Contraction of the right chart and expansion of the left.
   - Right esotropia: note that the fixation spot of the right inner chart is deviated nasally.
   - Right chart shows marked underaction of the lateral rectus and slight overaction of the medial rectus.
   - Left chart shows overaction of the medial rectus.

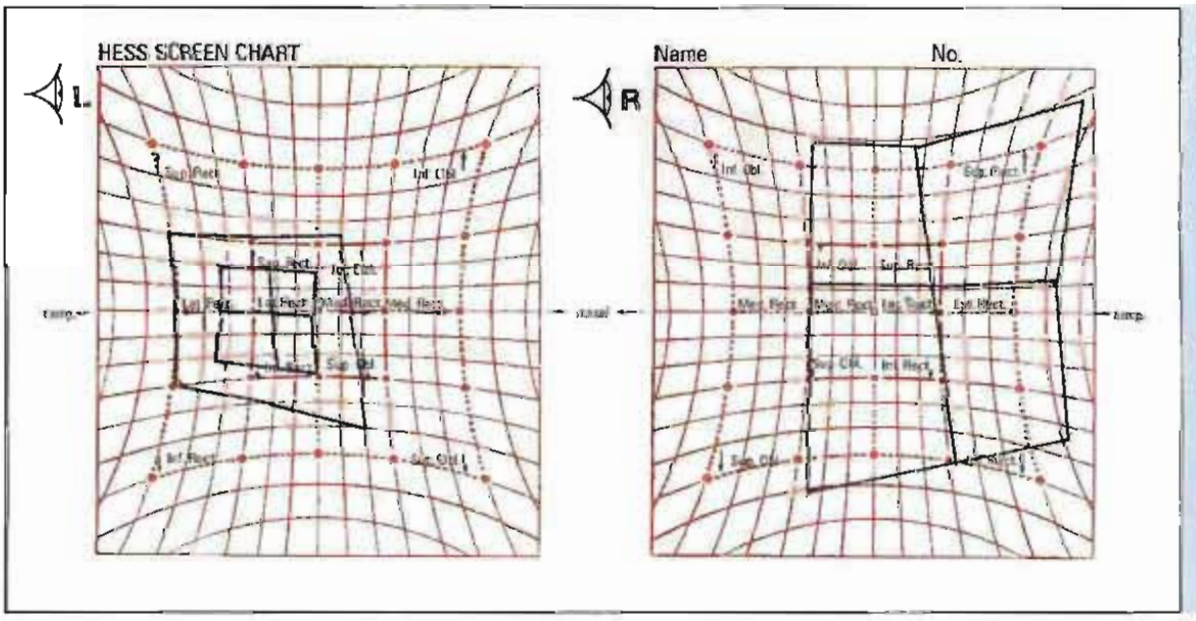

Fig. 16.57
Hess chart of a left third nerve palsy (see text)

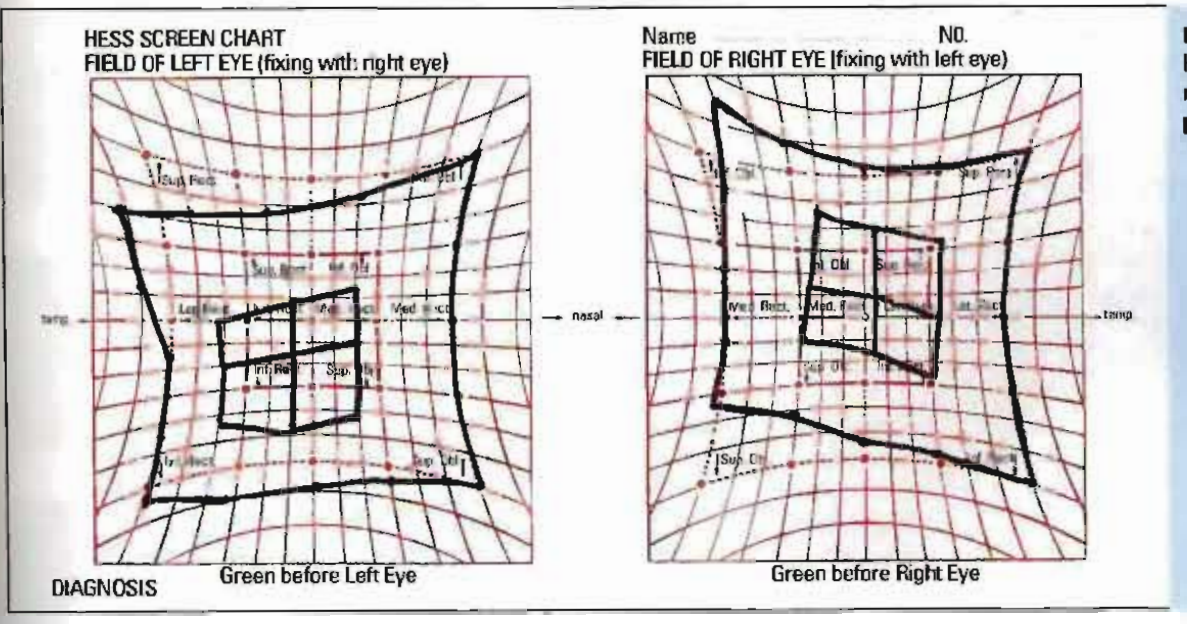

Fig. 16.58 Hess chart of a right fourth nerve palsy (see *text*)

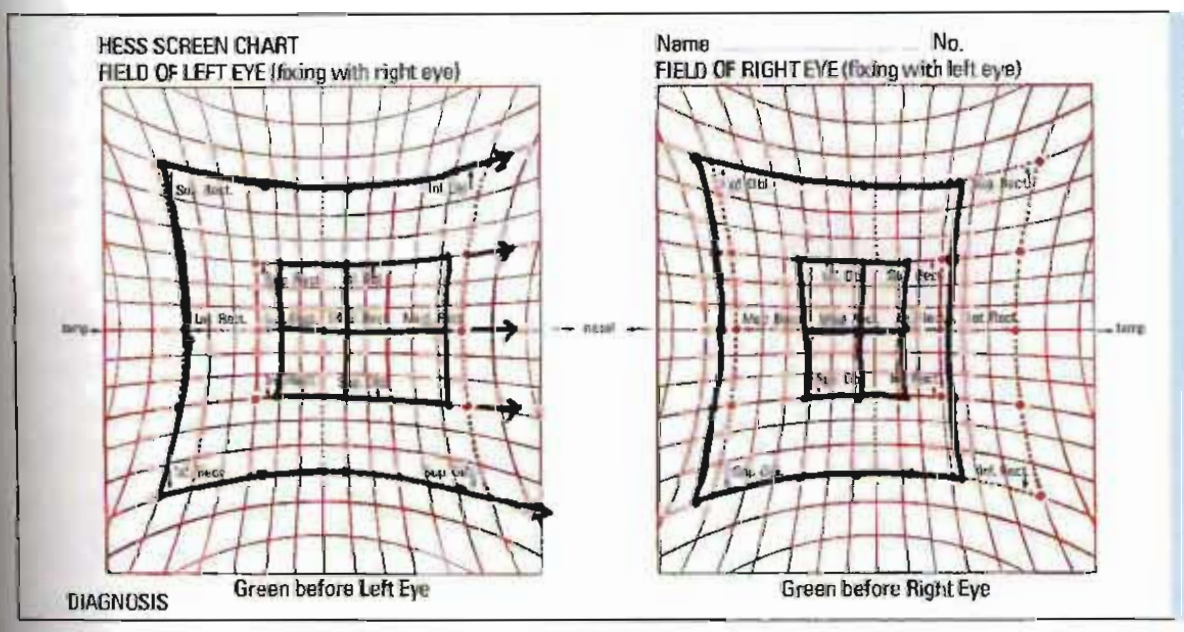

Fig. 16.59 Hess chart of a right sixth nerve palsy (see *text*)

Esotropia

Esotropia (manifest convergent squint) may be comitant or incomitant. In a comitant esotropia the variability of the angle of deviation is within 5 Δ in different horizontal gaze positions. In an incomitant deviation the angle differs in various positions of gaze as a result of abnormal innervation or restriction. Incomitant deviations are discussed later and this section deals only with comitant esotropia. The classification is shown in Table 16.1.

Accommodative esotropia

Near vision involves both accommodation and convergence. Accommodation is the process by which the eye focuses on a near target, by altering the curvature of the crystalline lens. Simultaneously, the eyes converge, in order to fixate bifoveally on the target. Both accommodation and convergence are quantitatively related to the proximity of the target, and have a fairly constant relationship to each other (AC/A ratio) as described previously. Abnormalities of the AC/A ratio are an important cause of certain types of esotropia.

Table 16.1 Classification of esotropia

1. **Accommodative**
   - *a. Refractive*
     - fully accommodative
     - partially accommodative
   - *b. Non-refractive*
     - with convergence excess
     - with accommodation weakness
   - *c. Mixed accommodative*
2. **Non-accommodative**
   - essential infantile
   - microtropia
   - basic
   - convergence excess
   - convergence spasm
   - divergence insufficiency
   - divergence paralysis
   - sensory
   - consecutive
   - acute-onset
   - cyclic

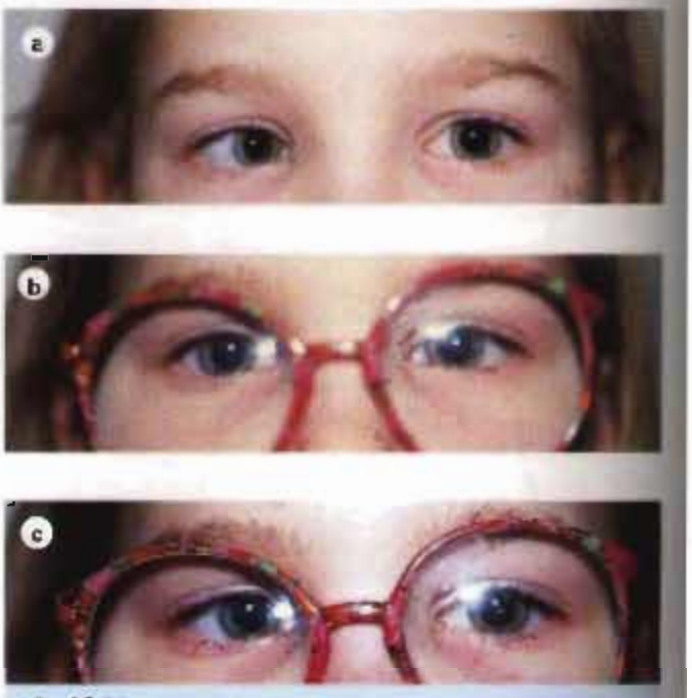

Fig. 16.61
Mixed accommodative esotropia. (a) Right esotropia; (b) Straight for distance with spectacle correction; (c) right esotropia for near with spectacle correction (Courtesy of K. Nischal)

Refractive accommodative esotropia

Here the AC/A ratio is normal and esotropia is a physiological response to excessive hypermetropia, usually between +4.00 and +7.00 D. The considerable degree of accommodation required to focus clearly on even a distant target is accompanied by a proportionate amount of convergence, which is beyond the patient's fusional divergence amplitude. It cannot therefore be controlled, and a manifest convergent squint results. The magnitude of the deviation varies little (usually <10 Δ) between distance and near. The deviation presents at about the age of 2.5 years (range of 6 months to 7 years).

1. **Fully accommodative** is completely eliminated by optical correction of hypermetropia (Fig. 16.60).
2. **Partially accommodative** is reduced, but not eliminated by correction of hypermetropia.

Non-refractive accommodative esotropia

This is associated with a high AC/A ratio in which a unit increase of accommodation is accompanied by a disproportionately large increase of convergence in the absence of significant hypermetropia. The two types are:

1. **Convergence excess**, which is characterized by:
   - High AC/A ratio due to increased AC (accommodation is normal, convergence is exaggerated).
   - Normal near point of accommodation.
   - Straight eyes for distance, but esotropia for near.
2. **With defective accommodation** (hypoaccommodative), which is characterized by:
   - High AC/A ratio due to decreased A (accommodation is weak, necessitating increased effort, which is accompanied by a strong convergence response).
   - Remote near point of accommodation.
   - Extra accommodative effort is required for near resulting in convergence excess.

Fig.16.60
Refractive fully accommodative esotropia. (a) Right esotropia; (b) straight eyes with spectacle correction (Courtesy of K. Nischal)

Mixed accommodative esotropia

Hypermetropia and a high AC/A ratio may coexist, resulting in esotropia for distance, which increases markedly (>10 Δ) on near fixation. The distance deviation is usually corrected by spectacles (Fig. 16.61a and b), but the patient will still have an esotropia for near (Fig. 16.61c), unless wearing bifocals.

Management

1. **Refractive error** should be corrected, as previously described. In children under the age of 6 years, the full cycloplegic refraction revealed on retinoscopy should be prescribed (with a deduction only for the working distance). In the fully accommodative refractive esotrope this will control the deviation for both near and distance. After the age of 8 years, retinoscopy should be performed without cycloplegia and the maximal amount of 'plus' that can be tolerated (the manifest hypermetropia) prescribed.
2. **Bifocals** may be prescribed if there is accommodative esotropia for near (high AC/A ratio). Bifocals relieve accommodation (and thereby accommodative convergence), thus allowing the child to maintain bi-foveal fixation/ocular alignment at near. The minimum 'plus' required to achieve this is used. The most satisfactory form of bifocals is the executive type in which the intersection crosses the lower border of the pupil. The strength of the lower segment should be gradually reduced and eliminated by the early teenage years. The ultimate prognosis for complete withdrawal of spectacles is related to the magnitude of the AC/A ratio and also the degree of hypermetropia and associated astigmatism. Spectacles may be needed only for close work.
3. **Miotic therapy** can be used short-term in children with accommodative esotropia due to a high AC/A ratio, who will not wear spectacles. The initial dose is 0.125% ecothiopate iodide once daily or 4% pilocarpine q.i.d. for 6 weeks. If this is effective, the strength and frequency can be gradually reduced to a minimal effective dose. The formation of iris cysts induced by ecothiopate can be prevented by the simultaneous administration of 2.5% phenylephrine drops twice daily. Miotic therapy works by inducing 'peripheral' accommodation (i.e. direct stimulation of the ciliary muscle rather than that mediated by the third cranial nerve). Less accommodative effort is therefore required by the patient for near vision and thereby less accommodative convergence is induced. It may, however, result in blurred distance vision.
4. **Treatment of amblyopia**, as previously described, is very important before contemplating surgery.
5. **Surgery** may be considered if spectacles do not fully correct the deviation, after every attempt has been made to treat amblyopia. The principle of surgery involves weakening of the medial recti, the muscles active in ocular convergence.
   - Bilateral medial rectus recessions are performed in patients with equal vision in both eyes, in which the deviation for near is greater than that for distance.
   - If there is no significant difference between distance and near measurements, and equal vision in both eyes, some perform medial rectus recession combined with lateral rectus resection, whereas others prefer bilateral medial rectus recessions.
   - Recession–resections on the amblyopic eye are performed in patients with residual amblyopia.

Essential infantile esotropia

Essential infantile esotropia is an idiopathic esotropia developing within the first 6 months of life in an otherwise normal infant with no significant refractive error and no limitation of ocular movements.

Signs

- The angle is usually fairly large (>30 Δ) and stable (Fig. 16.62).
- Fixation in most infants is alternating in the primary position and cross-fixating in side gaze, so that the child uses the right eye in left gaze (Fig. 16.63b) and the left eye in right gaze (Fig. 16.63a). Such cross-fixation may give a false impression of bilateral abduction deficits, such as with bilateral sixth nerve palsy. Abduction can, however, usually be demonstrated either by the doll's head manoeuvre or rotating the child. Should these fail, uniocular patching for a few hours will often unmask the ability of the other eye to abduct (Fig. 16.63c).
- Nystagmus, if manifest, is usually horizontal (it may be latent, or manifest-latent).
- The refractive error is usually normal for the age of the child (about +1.50 D).

Fig. 16.62
Essential infantile esotropia

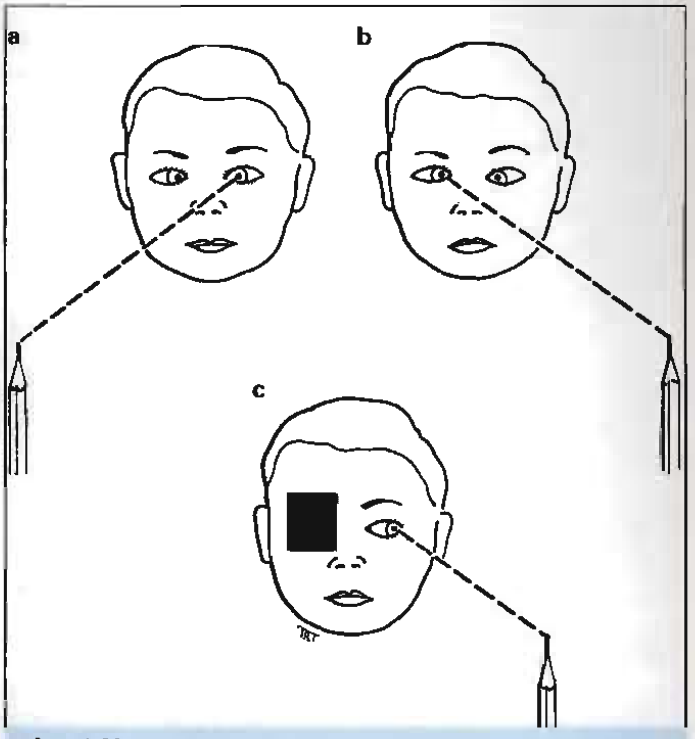

Fig. 16.63
Cross-fixation in essential infantile esotropia (Courtesy of Wilmer Institute)

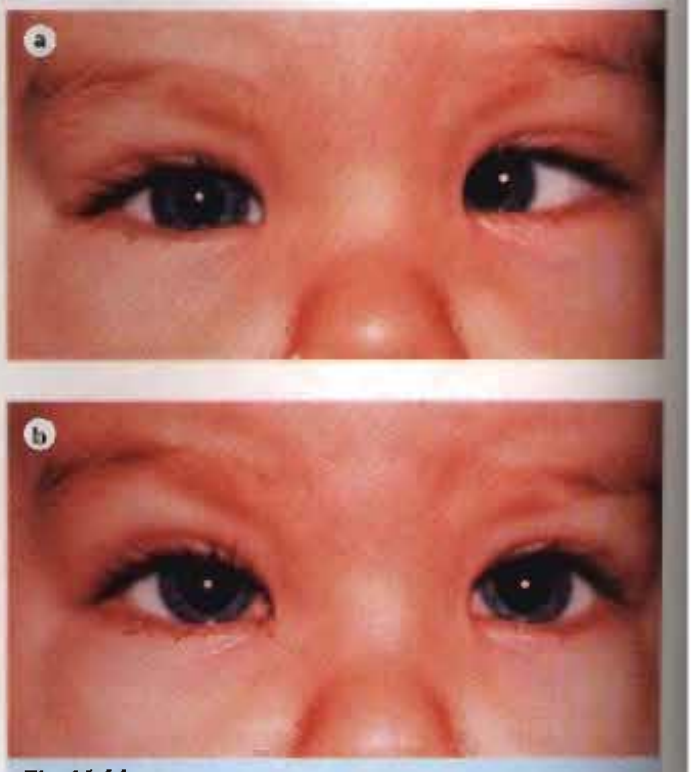

Fig. 16.64
(a) Essential infantile esotropia; (b) after appropriate surgery

- Asymmetry of optokinetic nystagmus.
- Inferior oblique overactions may be present initially or develop later.
- Dissociated vertical deviation develops in 80% by the age of 3 years (*see* below).
- Poor potential for BSV.

Differential diagnosis

- Congenital bilateral sixth nerve palsy, which can be excluded as described above.
- Sensory esotropia due to organic eye disease.
- Nystagmus blockage syndrome in which convergence dampens a horizontal nystagmus.
- Duane syndrome types I and III.
- Möbius syndrome.
- Strabismus fixus.

Initial management

Ideally, the eyes should be surgically aligned by the age of 12 months, and at the very latest by the age of 2 years, but only after amblyopia or significant refractive errors have been corrected. The initial procedure is recession of both medial recti. Very large angles may require recessions of 6.5 mm or more. Any associated overactions of the inferior obliques should also be addressed. An acceptable goal is alignment of the eyes to within 10 Δ esotropia, associated with peripheral fusion (combats diplopia) and central suppression (combats confusion) (Fig. 16.64). This small-angle residual strabismus is often stable, even though bifoveal fusion is not achieved.

Fig. 16.65
Left inferior oblique overaction

Subsequent management

1. **Undercorrection** may require further recession of the medial recti or resection of one or both lateral recti.
2. **Inferior oblique overaction** may develop subsequently, most commonly at age 2 years (Fig. 16.65). The parents should therefore be warned that further surgery may be necessary despite an initially good result. Initially unilateral, it frequently becomes bilateral within 6 months. Inferior oblique weakening procedures include myotomy, myectomy and recession (*see* later).
3. **Dissociated vertical deviation** (DVD) may appear several years after the initial surgery, particularly in children with nystagmus. It is characterized by the following:

Fig. 16.66
Dissociated vertical deviation (*see text*)

- Up-drift with excyclodeviation of the eye when under cover or during periods of visual inattention (Fig. 16.66).
- When the cover is removed the affected eye will move down without a corresponding down-drift of the other eye. Thus DVD does not obey Hering law. Although it is usually bilateral, it may be asymmetrical. Surgical treatment is indicated when the condition is cosmetically unacceptable. Superior rectus recession with or without a Faden procedure (*see* later) and/or inferior oblique anterior transposition are popular operations for DVD, although full correction is seldom possible.

4. **Amblyopia** subsequently develops in about 50% of cases.
5. **An accommodative element** should be suspected if the eyes are initially straight, or almost straight after surgery and then start to reconverge. It is therefore important to perform repeated refractions on all children and to correct any new accommodative elements accordingly.

Microtropia

Microtropia (monofixation syndrome) may be primary or follow surgery for a large deviation.

Signs

1. **Anisometropia** in nearly all cases, commonly with hypermetropia or hypermetropic astigmatism.
2. **Very small angle** measuring 8 Δ or less, which may or may not be detectable on cover testing (Fig. 16.67).
3. **Central suppression scotoma** of the deviating eye that prevents confusion may be detected by the following:

Fig. 16.67
Right microtropia

   a. ***Bagolini striated glasses*** in which a cross may be seen but there is a gap in the oblique line perceived by the microtropic (scotomatous) eye, at the point of intersection (*see* Fig. 16.32d).
   b. ***4Δ base-out test***
      - When a 4Δ base-out prism is placed in front of a normal eye, the sudden displacement of the image from the fovea to a parafoveal temporal point on the retina will elicit a refixation movement.
      - No movement will be seen in a microtropic eye, since the image is shifted within the central suppression scotoma.
      - In accordance with Hering law, the fellow eye moves outward when the eye under the prism refixates and subsequently performs a slow fusional movement in the opposite direction to correct for its image displacement.
      - If a central scotoma has impaired foveal function, neither movement occurs.
4. **Other features** include ARC, normal or almost normal peripheral fusional amplitudes and reduced stereopsis.

Treatment

This consists of spectacle correction of anisometropia and occlusion for amblyopia but is almost never successful in restoring bifoveal fixation.

Other non-accommodative esotropias

Basic

1. **Signs**
   - No significant refractive error.
   - Deviation is equal for near and distance.
2. **Treatment** is surgical.

Convergence excess

1. **Signs**
   - No significant refractive error.
   - Orthophoria or small esophoria for distance.

- Esotropia for near but normal or low AC/A ratio.
- Normal near point of accommodation.

2. **Treatment** involves bilateral medial rectus recessions.

Cyclic oculomotor spasm

This is an intermittent phenomenon which is usually hysterical but may occasionally have an organic cause such as trauma or a posterior fossa tumour.

1. **Signs** during an attack are:
   - Esotropia due to sustained convergence.
   - Pseudo-myopia due to accommodative spasm.
   - Bilateral miosis.
2. **Treatment** is with cycloplegics and bifocals.

Divergence insufficiency

This typically affects healthy young adults.

1. **Signs**
   - Intermittent or constant esotropia for distance.
   - Minimal or no deviation for near.
   - Full abduction bilaterally.
   - Fusional divergence amplitudes may be reduced.
   - Absence of neurological disease.
2. **Treatment** is with prisms until spontaneous resolution or bilateral lateral rectus resections in persistent cases.

Divergence paralysis

This may present at any age and may be difficult to differentiate from unilateral or bilateral sixth nerve palsy, but is usually comitant. It is characterized by:

- Esotropia which is unchanged or may decrease on laterоversion, unlike a sixth nerve palsy.
- Fusional divergence amplitudes are either severely reduced or absent.
- Underlying neurological disease is present such as head trauma, intracranial space-occupying lesions and cerebrovascular accidents.

Sensory esotropia

This is caused by a unilateral reduction in visual acuity which interferes with or abolishes fusion, such as cataract, optic atrophy or hypoplasia, toxoplasma retinochoroiditis or retinoblastoma.

> ***NB:*** Fundus examination under mydriasis is therefore essential in all children with strabismus.

Consecutive esotropia

This follows surgical overcorrection of an exodeviation. Unless the deviation is very large, surgery should be postponed for several months because spontaneous improvement may occur.

Acute-onset esotropia

This is usually due to a sudden decompensation of esophoria or microtropia. The patient complains of diplopia and it is important to exclude sixth nerve palsy or divergence paralysis.

Cyclic esotropia

This is a very rare condition characterized by alternating manifest esotropia and orthophoria, each lasting 24 hours. The condition may persist for months or years and the patient may eventually develop a constant esotropia requiring surgery.

Exotropia

Exotropia (manifest divergent squint) may be constant or intermittent (Table 16.2)

Constant exotropia

Congenital exotropia

1. **Presentation** is at birth, in contrast to infantile esotropia.
2. **Signs**
   - Normal refraction.
   - Large and constant angle.
   - DVD may be present.
3. **Neurological anomalies** are frequently present, in contrast to infantile esotropia.
4. **Treatment** is mainly surgical and consists of bilateral lateral rectus recessions, usually combined with resection of one or both medial recti, depending on the angle.

Other types

1. **Sensory** exotropia is the result of monocular or binocular visual impairment by acquired lesions, such as cataract or other opacities of the media, in children over the age of 5 years or in adults (Fig. 16.68). Treatment consists of correction of the visual deficit, if possible, followed by surgery, if necessary.

Table 16.2 Classification of exotropia

1. **Constant**
   - congenital
   - sensory
   - consecutive
2. **Intermittent**
   - basic
   - convergence weakness
   - divergence excess

Fig. 16.68
Left sensory exotropia due to a dense cataract

2. **Consecutive** exotropia follows surgical correction of an esodeviation.

Intermittent exotropia

1. **Presentation** is most frequently at around 2 years with exophoria, which breaks down to exotropia under conditions of visual inattention, bright light (resulting in reflex closure of the affected eye), fatigue or ill health. With the passage of time, the deviation tends to become less well controlled.
2. **Clinical types**
   a. *Basic* exotropia where the angle of deviation is the same for distance and near fixation (Fig. 16.69).
   b. ***Convergence weakness*** tends to occur in older children and adults. The angle of deviation is greater for near fixation (Fig. 16.70). It may be associated with acquired myopia.
   c. ***Divergence excess***, in which the angle of deviation is greater for distance (Fig. 16.71). This type of exotropia may be true or simulated.

Fig. 16.69
Basic exotropia. Equal deviation for distance (a) and near (b) (Courtesy of Wilmer Institute)

Fig. 16.70
Convergence weakness exotropia. Greater deviation for near (b) than distance (a) (Courtesy of Wilmer Institute)

Fig. 16.71
Divergence excess exotropia. Greater deviation for distance (a) than near (b) (Courtesy of Wilmer Eye Institute)

- True type in which the angle for near is consistently less than that for distance.
- Simulated type is associated with a high AC/A ratio. The deviations for near and distance are similar when the near angle is remeasured with the patient looking through a +3.00 D lens or after a period of uniocular occlusion.

Management

1. **Spectacle correction** in myopic patients may, in some cases, control the deviation by stimulating accommodation and, with it, convergence.
2. **Orthoptic treatment** consisting of occlusion therapy, diplopia awareness and improvement of fusional convergence may also be useful in selected cases.
3. **Surgery** is necessary in most patients by about the age of 5 years. Some advocate recessions of both lateral recti,

whereas others recommend bilateral surgery only for those patients with divergence excess, preferring recession–resection where the distance–near measurements are the same.

Special syndromes

Duane syndrome

The hallmark of Duane syndrome is retraction of the globe on attempted adduction caused by co-contraction of the medial and lateral recti. The condition is often bilateral, although frequently involvement of one eye may be so subtle as to go unnoticed. Some children have associated congenital defects: the most common is perceptive deafness with associated speech disorder.

Classification (Huber)

1. **Type I**, the most common, is characterized by:
   - Limited or absent abduction.
   - Normal or mildly limited adduction.
   - In the primary position, straight or slight esotropia.
2. **Type II**, the least common, is characterized by:
   - Limited adduction.
   - Normal or mildly limited abduction.
   - In primary position, straight or slight exotropia.
3. **Type III**, is characterized by:
   - Limited adduction and abduction.
   - In the primary position, straight or slight esotropia.

Other features

Features that may occur in each of the three subgroups include the following:

- On attempted adduction there is retraction of the globe, produced by co-contraction of the medial and lateral recti, with resultant narrowing of the palpebral fissure (Fig. 16.72a). The degree of globe retraction may vary from gross to almost imperceptible. On attempted abduction, the palpebral fissure opens and the globe assumes its normal position (Fig. 16.72b).
- An up-shoot or down-shoot in adduction is seen in some patients. It has been suggested that this is a 'bridle' or 'leash' phenomenon, produced by a tight lateral rectus muscle which slips over or under the globe and produces an anomalous vertical movement of the eye. However, recent studies with MRI have shown that this is not always the case.

Management

In most cases the eyes are straight in the primary position and there is no amblyopia. Surgery is indicated if the eyes are not straight in the primary position and the patient has to adopt an abnormal head posture to achieve fusion. Surgery may also be necessary for cosmetically unacceptable up-shoots, down-shoots or severe globe retraction. Amblyopia, when present, is usually the result of anisometropia rather than strabismus.

Fig. 16.72
Left Duane retraction syndrome (see *text*) (Courtesy of Wilmer Institute)

> ***NB:*** The lateral rectus of the involved side should not be resected, as this increases retraction.

Brown syndrome

Brown syndrome is usually congenital but occasionally may be acquired:

Classification

1. **Congenital**
   - Idiopathic.
   - Congenital click syndrome where there is impaired movement of the superior oblique tendon through the trochlea.
2. **Acquired**
   - Iatrogenic damage to the trochlea or superior oblique tendon.
   - Inflammation of the tendon which may be caused by rheumatoid arthritis, pansinusitis and scleritis.

Clinical features

A right Brown syndrome has the following characteristics:

1. **Major signs**
   - Usually straight in the primary position (Fig. 16.73a).
   - Limited right elevation in adduction and occasionally also in the midline (Fig. 16.73b).
   - Usually normal right elevation in abduction (Fig. 16.73c).
   - Minimal or no superior oblique overaction.
   - Positive forced duction test on elevating the globe in adduction.

Fig. 16.73
Right Brown syndrome (see text)

2. **Variable signs**
   - Down-shoot in adduction.
   - Hypotropia in primary position.
   - Anomalous head position with ipsilateral tilt and chin elevation.

Differential diagnosis

1. **Inferior oblique palsy** has more vertical deviation in the primary position, superior oblique overaction, 'A' pattern and negative forced duction test.

2. **Monocular elevation deficit** is characterized by inability to elevate one eye in any position (Fig. 16.74).

Management

1. **Congenital** cases do not usually require treatment. Indications for surgery include primary position hypotropia and/or an anomalous head posture. The recommended procedure for congenital cases is superior oblique weakening.

Fig. 16.74
Right monoelevation deficit showing defective elevation in all positions

2. **Acquired** cases may benefit from steroids, either orally or by injection near the trochlea, together with treatment of the underlying cause.

Möbius syndrome

Möbius syndrome is a very rare congenital, sporadic condition.

1. **Ocular features**
   - Horizontal gaze palsy is present in 50% of cases but vertical gaze is usually intact.
   - Bilateral sixth nerve palsies (Fig. 16.75a).
   - Esotropia in the primary position in 50% of cases; the remainder are straight.
   - A pseudo-esotropia may be seen in children who learn to cross-fixate because adduction and convergence are intact.
2. **Systemic features**
   - Bilateral facial palsy, which is usually asymmetrical and often incomplete, giving rise to a mask-like facial expression and problems with lid closure (Fig. 16.75b).
   - Paresis of the ninth and twelfth cranial nerves. The latter results in atrophy of the tongue (Fig. 16.75c).
   - Mild mental handicap.
   - Limb anomalies.

Fibrosis syndromes

1. **Strabismus fixus** is a very rare condition, in which both eyes are fixed, by fibrous tightening of the medial recti (convergent strabismus fixus), or the lateral recti (divergent strabismus fixus).
2. **Congenital fibrosis of extraocular muscles syndrome** is a rare, autosomal-dominant, non-progressive disorder characterized by hypoplasia and fibrosis of extraocular muscles. It is characterized by bilateral congenital ptosis and restrictive external ophthalmoplegia. In the 'primary' position each eye is fixed below the horizontal, by about 10°. The hypotropic eye may be secondarily exotropic (Fig. 16.76), esotropic or neutral.

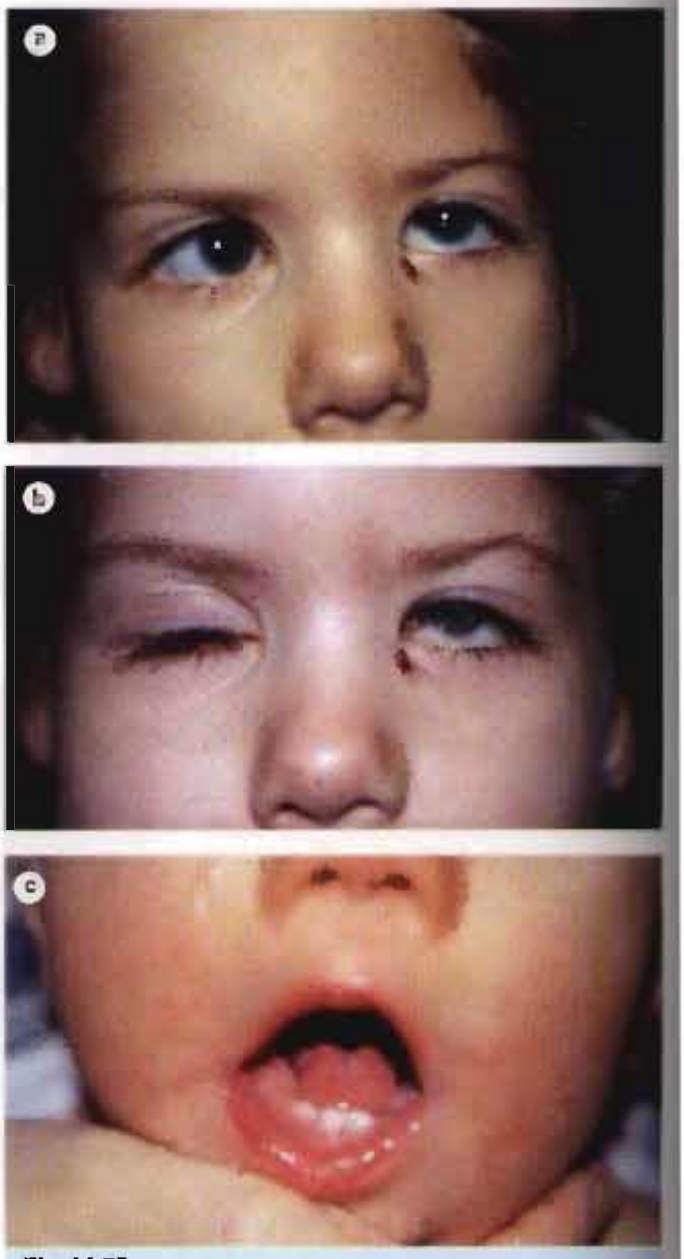

Fig. 16.75
Möbius syndrome. (a) Defective left abduction due to a sixth nerve palsy; (b) facial palsy; (c) atrophic tongue (Courtesy of K Nischal)

Fig. 16.76
Exotropia in congenital fibrosis of extraocular muscle syndrome (Courtesy of Wilmer Institute)

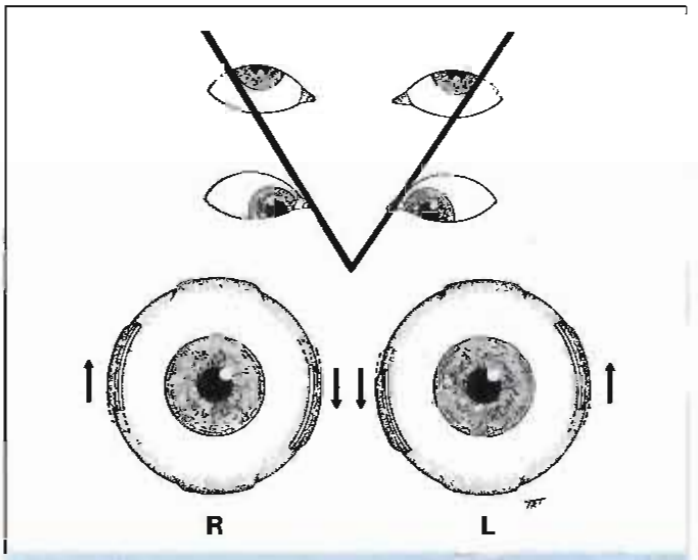

Fig. 16.77
Treatment of 'V' pattern by downward transposition of the medial recti or upward transposition of the lateral recti (see *text*)

The degree of residual horizontal movement varies from full to completely restricted. However, vertical movements are always severely restricted with inability to elevate the eyes above the horizontal plane.

Alphabet patterns

Horizontal deviations can vary when measured in the primary position, upgaze and downgaze, regardless of whether a deviation is comitant or incomitant.

'V' pattern

'V' pattern is significant when difference between upgaze and downgaze is >15 Δ.

Causes

- Brown syndrome.
- Inferior oblique overaction associated with fourth nerve palsy.
- Superior oblique underaction with subsequent inferior oblique overaction which is seen in infantile esotropia as well as other childhood esotropias. The eyes are often straight in upgaze, with a marked esodeviation in downgaze.
- Superior rectus underaction.
- Lateral rectus overaction.
- Craniofacial anomalies which are associated with shallow orbits and downslanting palpebral fissures. There is often a gross exotropia in upgaze and the eyes are almost straight in downgaze.

Fig. 16.78
'V' pattern esotropia (Courtesy of Wilmer Institute)

Treatment

Without oblique muscle dysfunction (Fig. 16.77):

1. **'V' pattern esotropia** (Fig. 16.78) is treated by bilateral medial rectus recessions and downward transposition of the tendons.
2. **'V' pattern exotropia** (Fig. 16.79) is treated by bilateral lateral rectus recessions and upward transposition.

'A' pattern

'A' pattern is significant if the difference between upgaze and downgaze is >10 Δ.

Fig. 16.79
'V' pattern exotropia (Courtesy of Wilmer Institute)

Fig. 16.81
'A' pattern esotropia (Courtesy of Wilmer Institute)

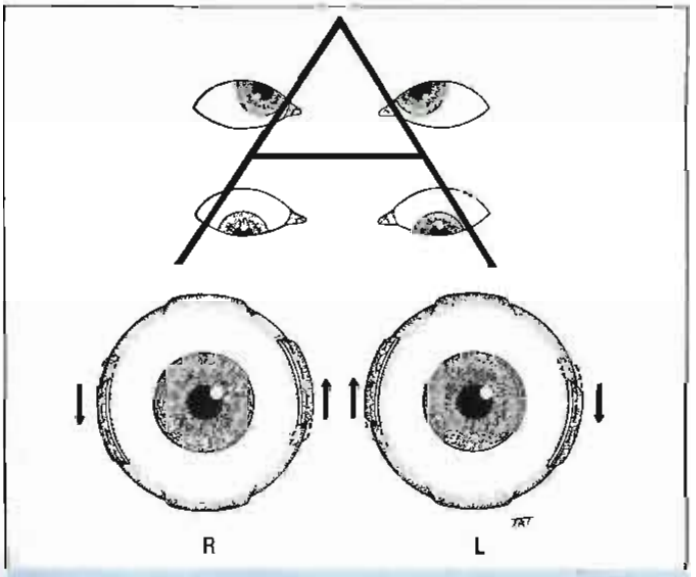

Fig. 16.80
Treatment of 'A' pattern by upward transposition of medial recti or downward transposition of lateral recti (see text)

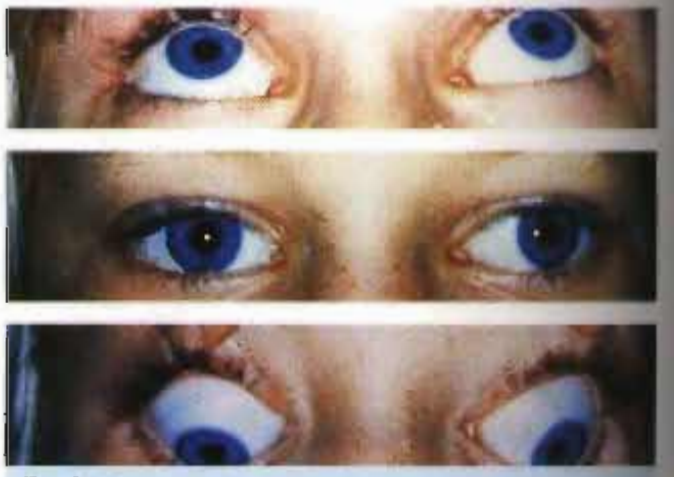

Fig. 16.82
'A' pattern exotropia (Courtesy of Wilmer Institute)

Causes

- Primary superior oblique overaction which is usually associated with exodeviation in the primary position of gaze.
- Inferior oblique underaction/palsy with subsequent superior oblique overaction.
- Lateral rectus underaction.
- Inferior rectus underaction.

Treatment

Without oblique muscle dysfunction (Fig. 16.80):

1. **'A' pattern esotropia** (Fig. 16.81) is treated by bilateral medial rectus recessions and upward transposition.
2. **'A' pattern exotropia** (Fig. 16.82) is treated by bilateral lateral rectus recessions and downward transposition.

Principles of surgery

The aims of surgery on the extraocular muscles are to correct misalignment and, if possible, restore BSV. However, the first step in the management of childhood strabismus involves correction of any significant refractive error and/or amblyopia. Once maximal visual potential is reached in both eyes, any residual deviation can be treated surgically. The three main types of procedures are: (a) *weakening*, which decreases the pull of a muscle, (b) *strengthening*, which enhances the pull of a muscle, and (c) those that *change the direction of muscle action*.

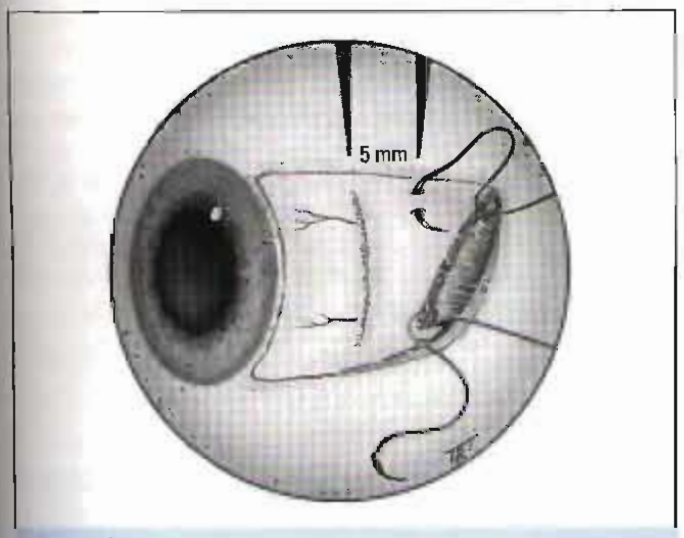

Fig. 16.83
Horizontal rectus muscle recession

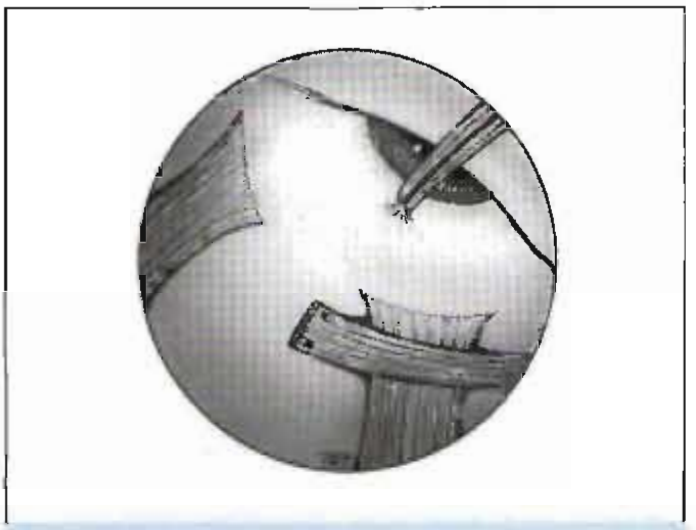

Fig. 16.84
Inferior oblique recession

Weakening procedures

The procedures for weakening the action of a muscle are: (a) *recession*, (b) *myectomy* and (c) *posterior fixation suture*.

Recession

This slackens a muscle by moving its insertion towards its origin. It can be performed on any muscle except the superior oblique.

1. **Rectus muscle recession**
   a. The muscle is exposed and two absorbable sutures passed through the outer quarters of the tendon.
   b. The tendon is disinserted from the sclera, and the amount of recession is measured and marked on the sclera with calipers.
   c. The stump is resutured to the sclera posterior to its original insertion (Fig. 16.83).
2. **Inferior oblique recession**
   a. The muscle belly is exposed through an inferotemporal fornix incision.
   b. One or two absorbable sutures are passed through the muscle near its insertion.
   c. The muscle is disinserted and the stump resutured to the sclera, 2 mm posterior and temporal to the temporal edge of the inferior rectus insertion (Fig. 16.84).

Myectomy

This involves severing the muscle from its insertion without reattachment. It is most commonly used in weakening an overacting inferior oblique muscle. Very occasionally, the procedure is performed on a severely contracted rectus muscle.

Posterior fixation suture

The principle of this (Faden) procedure is to decrease the pull of the muscle in its field of action without affecting it in the primary position. The Faden procedure may be used to treat DVD, although it can also be used to weaken a horizontal rectus muscle. When treating DVD, the superior rectus muscle is usually first recessed. The belly of the muscle is then anchored to the sclera with a non-absorbable suture about 12 mm behind its insertion.

Strengthening procedures

1. **Resection** shortens a muscle to enhance its effective pull. It is suitable only for a rectus muscle and invoives the following steps:

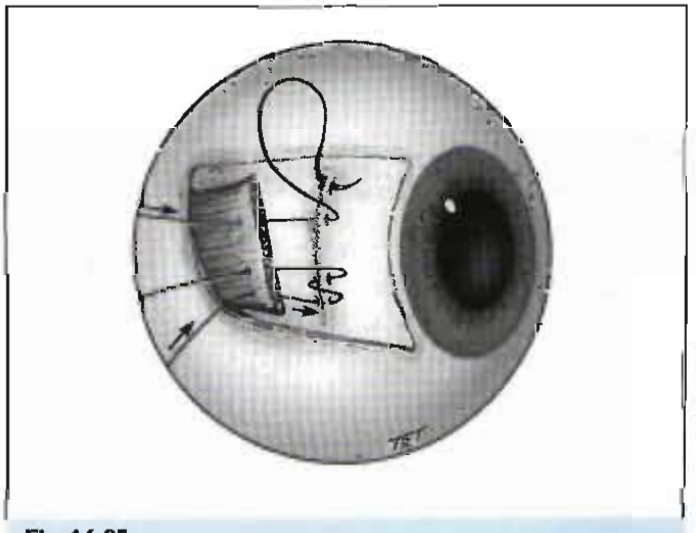

Fig. 16.85
Horizontal rectus muscle resection

a. The muscle is exposed and two absorbable sutures are inserted into the muscle at a predetermined point behind its insertion.
b. The muscle anterior to the sutures is excised and the stump is reattached to the original insertion (Fig. 16.85).

2. **Tucking** of a muscle or its tendon is usually reserved to enhance the action of the superior oblique muscle in congenital fourth nerve palsy.
3. **Advancement** of the muscle nearer to the limbus can be used to enhance the action of a previously recessed rectus muscle.

Treatment of paretic strabismus

Lateral rectus palsy

Surgical intervention for a sixth nerve palsy should be considered only when it is apparent that spontaneous improvement will not occur. This is usually after 6 months have elapsed. The two main procedures aimed at improving abduction are the following:

1. **Hummelsheim procedure**
   a. The medial rectus is recessed.
   b. The lateral halves of the superior and inferior recti are disinserted and reattached to the superior and inferior margins of the paretic lateral rectus muscle (Fig. 16.86a).

> *NB:* As this procedure involves detaching three rectus muscles from the globe, there is a risk of postoperative anterior segment ischaemia. To avoid this complication, the medial rectus recession may be replaced with botulinum toxin chemodenervation (see later).

2. **Jensen procedure** is also used to improve abduction and is combined with recession of or injection of botulinum toxin into the medial rectus muscle.
   a. The superior, lateral and inferior recti are split lengthways.
   b. With a non-absorbable suture, the lateral half of the superior rectus is tied to the superior half of the lateral rectus, and the inferior half of the lateral rectus is tied to the lateral half of the inferior rectus (Fig. 16.86b).

Superior oblique palsy

Surgical intervention should be considered in cases of abnormal head posture and diplopia unresponsive to prisms. General principles are as follows:

1. **Congenital** cases with a large hypertropia in the primary position are treated by superior oblique tucking.
2. **Acquired**
   a. Small hypertropias are treated by ipsilateral inferior oblique weakening.
   b. Moderate to large acquired hypertropias may be treated by ipsilateral inferior oblique weakening combined with ipsilateral superior rectus weakening and/or contralateral inferior rectus weakening. It should be noted that weakening the inferior oblique and superior rectus of the same eye may result in defective elevation.
   c. Pure excyclotropias, without hypertropia, are treated by the Harada–Ito procedure, which involves splitting and anterolateral transposition of the lateral half of the superior oblique tendon (Fig. 16.87).

Adjustable sutures

Indications

In certain cases, the results of strabismus surgery can be improved by the use of adjustable suture techniques. These

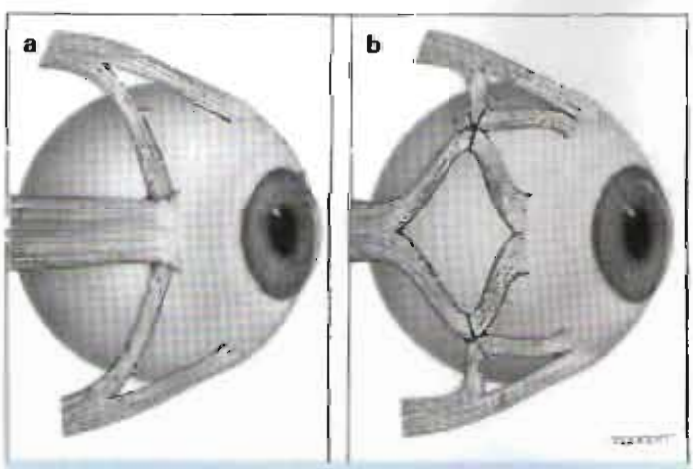

Fig. 16.86
Treatment of lateral rectus palsy. (a) Hummelsheim procedure; (b) Jensen procedure

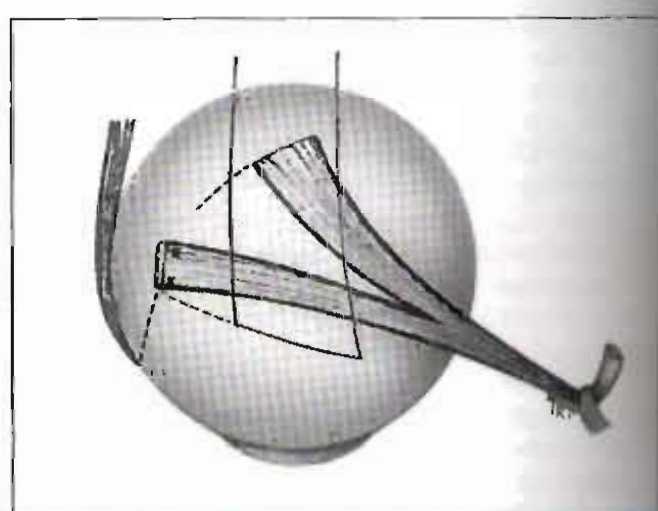

Fig. 16.87
Harada–Ito procedure for superior oblique palsy

are particularly indicated when a precise outcome is essential and when the results with more conventional procedures are likely to be unpredictable; for example, acquired vertical deviations associated with thyroid myopathy or following a blow-out fracture of the floor of the orbit. Other relative indications include sixth nerve palsy, adult exotropia and reoperations in which scarring of surrounding tissues may make the final outcome unpredictable. The main contraindication is a patient who is too young or unwilling to cooperate during postoperative suture adjustment.

Initial steps

1. The muscle is exposed, sutures inserted and the tendon disinserted from the sclera (as for a rectus muscle recession).
2. The two ends of the suture are passed, close together, through the stump of the insertion.
3. A second suture is knotted and tied tightly around the muscle suture anterior to its emergence from the stump (Fig. 16.88a).
4. One end of this suture is then cut short and the two ends tied together to form a loop (Fig. 16.88b).
5. The conjunctiva is left open.

Postoperative adjustment

1. The extent of alignment is assessed.
2. If ocular alignment is satisfactory the muscle suture is tied and its long ends cut short.
3. If more recession is required, the knot is pulled anteriorly along the muscle suture, thereby providing additional slack to the recessed muscle and enabling it to move posteriorly (Fig. 16.88c).
4. If less recession is required, the muscle suture is pulled anteriorly and the knot pulled against the muscle stump (Fig. 16.88d).
5. The conjunctiva is closed.

A similar technique is used for rectus muscle resection.

Botulinum toxin chemodenervation

Temporary paralysis of an extraocular muscle can be created in conjunction with the transposition procedures as already described or in isolation. The following are the main indications for considering chemodenervation:

- To determine function of the lateral rectus in a sixth nerve palsy where medial rectus contracture prevents any abduction. A tiny dose of botulinum toxin B is injected into

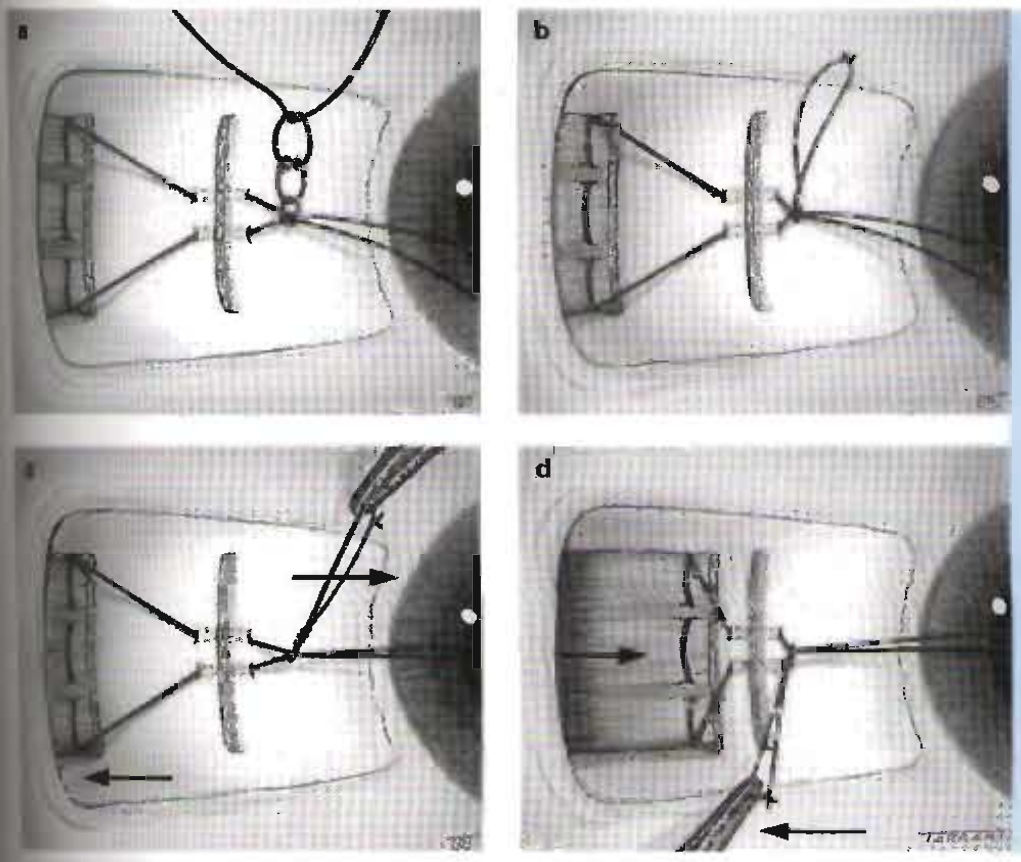

Fig. 16.88
Adjustable sutures (see *text*)

the belly of the overacting antagonist (medial rectus) under electromyographic guidance (Fig. 16.89a). The temporary paralysis of the muscle causes relaxation so that the horizontal forces on the globe are more balanced, thus allowing assessment of lateral rectus function (Fig. 16.89b).

- To determine the risk of postoperative diplopia and to assess the potential for BSV. For example, in an adult with a left divergent strabismus and good vision in both eyes, the left lateral rectus muscle can be injected so that the eyes will either straighten or converge.
- However, placing a corrective prism in front of the deviating eye offers a simpler, and perhaps more accurate method of determining the risk of postoperative diplopia.

If either of the above indicates the likelihood of diplopia, the patient can then be advised preoperatively of this possibility. Such diplopia, however, almost invariably resolves spontaneously.

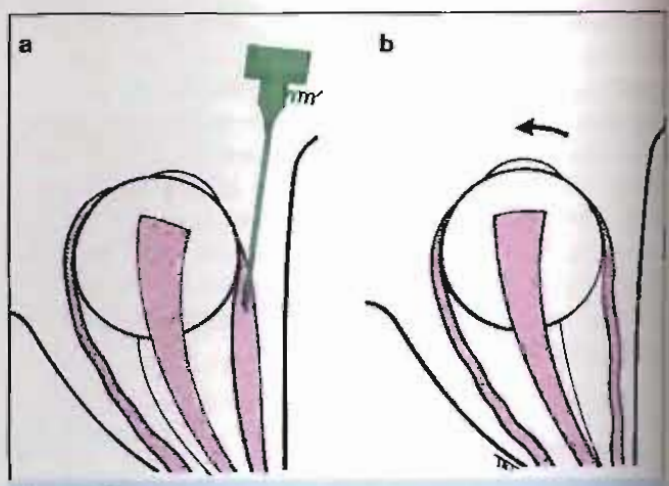

Fig. 16.89
Principles of botulinum toxin chemodenervation in left sixth nerve palsy (see *text*)

CHAPTER 17

Orbit

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Introduction

Applied anatomy

The orbit is a pear-shaped cavity, the stalk of which is the optic canal (Fig. 17.1). The intraorbital portion of the optic nerve is longer (25 mm) than the distance between the back of the globe and the optic canal (18 mm). This allows for significant forward displacement of the globe (proptosis) without excessive stretching of the optic nerve.

1. **The roof** consists of *two* bones: lesser wing of the sphenoid and the orbital plate of the frontal. It is located subjacent to the anterior cranial fossa and frontal sinus. A defect in the orbital roof may cause pulsatile proptosis as a result of transmission of cerebrospinal fluid pulsation to the orbit.
2. **The lateral wall** also consists of *two* bones: greater wing of the sphenoid and zygomatic. The anterior half of the globe is vulnerable to lateral trauma since it protrudes beyond the lateral orbital margin.
3. **The floor** consists of *three* bones: zygomatic, maxillary and palatine. The posteromedial portion of the maxillary bone is relatively weak and may be involved in a 'blow-out' fracture. The orbital floor also forms the roof of the maxillary sinus, so that maxillary carcinoma invading the orbit may displace the globe upwards.
4. **The medial wall** consists of *four* bones: maxillary, lacrimal, ethmoid and sphenoid. The lamina papyracea, which forms part of the medial wall, is paper-thin and perforated by numerous foramina for nerves and blood vessels. Orbital cellulitis is therefore frequently secondary to ethmoidal sinusitis.
5. **The superior orbital fissure** is a slit between the greater and lesser wings of the sphenoid bone through which pass important structures from the cranium to the orbit.
   - The superior portion contains the lacrimal, frontal and trochlear nerves and the superior ophthalmic vein.
   - The inferior portion contains the superior and inferior divisions of the oculomotor nerve, the abducens, the nasociliary and sympathetic fibres.

NB: Inflammation at the superior orbital fissure and orbital apex may therefore result in a multitude of signs including ophthalmoplegia and venous outflow obstruction resulting in oedema of the lids and proptosis.

Clinical signs of orbital disease

Soft tissue involvement

1. **Signs** include lid and periorbital oedema, ptosis, chemosis and conjunctival injection (Fig. 17.2).
2. **Causes** include thyroid eye disease, orbital cellulitis, inflammatory orbital disease and arteriovenous shunts.

Fig. 17.2
Soft tissue involvement in orbital disease

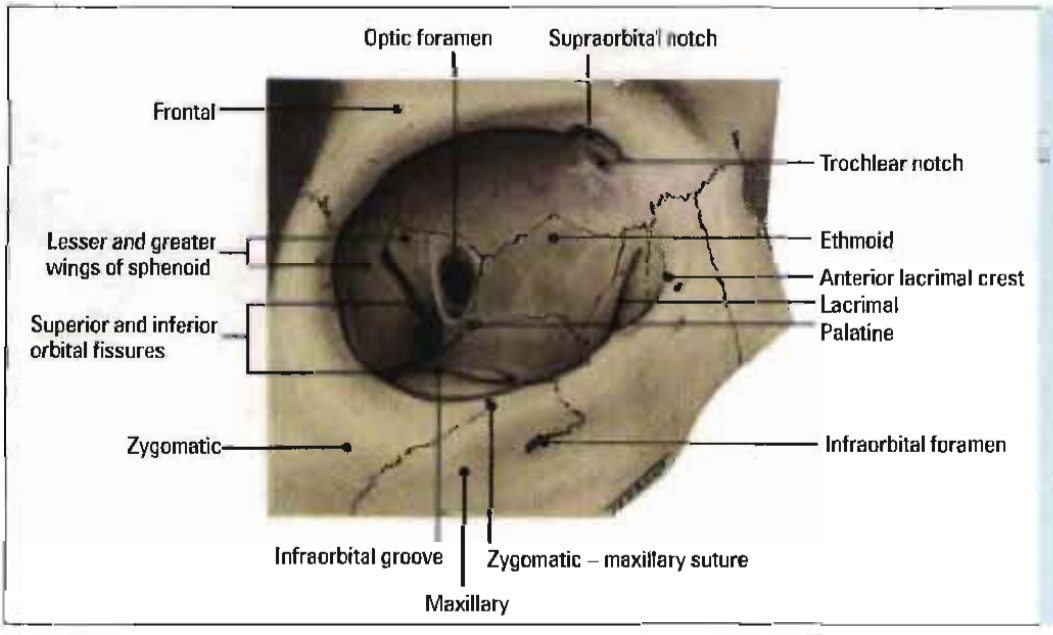


Fig. 17.1
Anatomy of the orbit

Fig. 17.3
Proptosis

Fig. 17.4
Measurement of globe protrusion with a plastic rule

Proptosis

This is an abnormal protrusion of the globe which may be caused by retrobulbar lesions or, less frequently, a shallow orbit. Asymmetrical proptosis is best detected by looking down at the patient from above and behind (Fig. 17.3). The following characteristics are relevant:

1. **The direction of proptosis** may indicate the possible pathology. For example, space-occupying lesions within the muscle cone, such as cavernous haemangiomas and optic nerve tumours, cause axial proptosis, whereas extraconal lesions usually give rise to eccentric proptosis, the direction of which is governed by the site of the mass.
2. **The severity of proptosis** can be measured with a plastic rule resting on the lateral orbital margin (Fig. 17.4) or a Hertel exophthalmometer, by means of which the corneal apices are visualized in the mirrors and the degree of ocular protrusion is read off a scale (Fig. 17.5). Ideally, measurements should be taken in both erect and supine positions. Readings greater than 20 mm are indicative of proptosis and a difference of 2 mm between the two eyes is suspicious regardless of the absolute value. Proptosis is graded as mild (21–23 mm), moderate (24–27 mm) and severe (28 mm or more). The dimensions of the palpebral apertures and any lagophthalmos should also be noted.
3. **Pseudo-proptosis** (false impression of proptosis) may be due to facial asymmetry, severe ipsilateral enlargement of the globe (e.g. high myopia or buphthalmos) (Fig. 17.6), ipsilateral lid retraction or contralateral enophthalmos (Fig. 17.7).

Dystopia

This implies displacement of the globe in the coronal plane, usually due to an extraconal orbital mass such as a lacrimal gland tumour (Fig. 17.8). It may coexist with proptosis or enophthalmos. Horizontal displacement is measured from

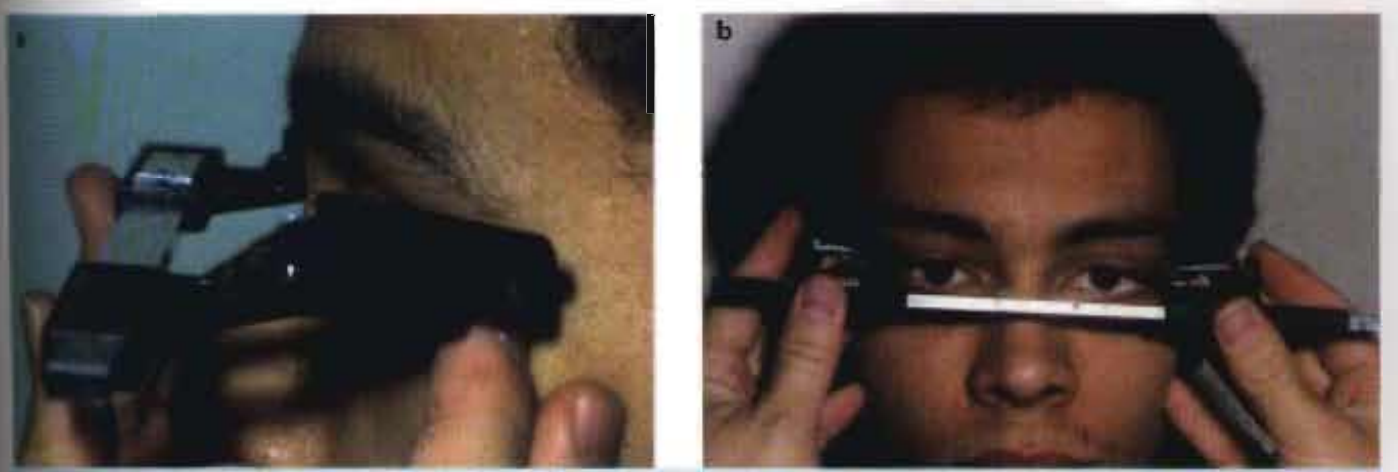


Fig. 17.5
Measurement of globe protrusion with a Hertel exophthalmometer

Fig. 17.6
Right pseudo-proptosis due to a combination of a large globe associated with very high myopia and phthisis of the left eye

Fig. 17.7
Mild left enophthalmos

Fig. 17.8
Left downward dystopia

Fig. 17.9
Right enophthalmos due to an orbital floor blow-out fracture

the midline (nose) to the nasal limbus, while vertical dystopia is read off a vertical scale perpendicular to a horizontal rule placed over the bridge of the nose. In the context of coexistent strabismus, it is essential to establish that the eye is fixating, if necessary by occluding the fellow eye, while measuring dystopia.

Enophthalmos

This implies recession of the globe within the orbit. Often subtle, it may be caused by the following mechanisms:

1. **Structural abnormalities** of the orbital walls may be post-traumatic, such as blow-out fractures of the orbital floor (Fig. 17.9), or congenital.
2. **Atrophy of orbital contents** may be secondary to radiotherapy, scleroderma or eye poking (oculodigital sign) in blind infants (*see* Fig. 15.33).
3. **Cicatrizing orbital lesions** such as metastatic schirrous carcinoma and chronic sclerosing inflammatory orbital disease.

NB: Pseudo-enophthalmos may be caused by microphthalmos or phthisis bulbi.

Ophthalmoplegia

Defective ocular motility may be caused by one or more of the following:

1. **An orbital mass.**
2. **Restrictive myopathy** in thyroid eye disease or orbital myositis.
3. **Ocular motor nerve lesions** associated with carotid-cavernous fistula, Tolosa–Hunt syndrome and malignant lacrimal gland tumours.
4. **Tethering** of extraocular muscles or fascia in a blow-out fracture.
5. **Splinting** of the optic nerve by an optic nerve sheath meningioma.

Restrictive versus neurological ophthalmoplegia

The following tests may be used to differentiate a restrictive from a neurological motility defect:

1. **The forced duction test**
   a. Topical anaesthetic drops are instilled.
   b. A cotton pledget soaked in anaesthetic is inserted into both eyes over the muscles to be tested and left for about 5 minutes.
   c. The insertion of the muscle in the involved eye is grasped with forceps and the globe is rotated in the direction of limited mobility.
   d. The test is repeated in the unaffected eye.
      (i) Positive result: difficulty or inability to move the globe indicates a restrictive problem such as thyroid myopathy or muscle entrapment in an orbital floor frac-

ture. In the opposite eye, no such resistance will be encountered unless pathology is bilateral.

(ii) *Negative result*: no resistance will be encountered in either eye if the muscle is paretic as a result of a neurological lesion.

2. **The differential intraocular pressure test**
   a. The intraocular pressure is measured in the primary position of gaze.
   b. The measurement is repeated with the patient attempting to look into the direction of limited mobility.
      (i) *Positive result*: an increase of 6 mmHg or more denotes resistance transmitted to the globe by muscle restriction.
      (ii) *Negative result*: an increase of <6 mmHg suggests a neurological lesion.

NB: The advantage of this test over the forced duction is less discomfort and an end-point that is objective rather than subjective.

3. **Saccadic eye movements** in neurological lesions are reduced in velocity, while restrictive defects manifest normal saccadic velocity with 'sudden halting' of ocular movement.

Causes of visual dysfunction

1. **Exposure keratopathy** secondary to severe proptosis, associated with lagophthalmos and impaired Bell phenomenon, is the most common.
2. **Compressive optic neuropathy** characterized by signs of optic nerve dysfunction such as impaired visual acuity, colour vision and contrast sensitivity, visual field defects, afferent conduction defects and optic disc changes (*see* Chapter 18).
3. **Choroidal folds** at the macula may occasionally affect vision.

Dynamic properties

The following dynamic features may give clues as to the probable pathology:

1. **Increasing venous pressure** by dependent head position, Valsalva manoeuvre or jugular compression may induce or exacerbate proptosis in patients with orbital venous anomalies or infants with capillary orbital haemangiomas.
2. **Pulsation** is caused either by an arteriovenous communication or a defect in the orbital roof.
   - In the latter the pulsation is transmitted from the brain by the cerebrospinal fluid and there is no associated bruit.
   - In the former pulsation may be associated with a bruit depending on the size of the communication.

NB: Mild pulsation is best detected on the slit-lamp, particularly when performing applanation tonometry.

3. **A bruit** is a sign of carotid–cavernous fistula. It is best heard with the bell of the stethoscope and is lessened or abolished by gently compressing the ipsilateral carotid artery in the neck.

Optic disc changes

1. **Optic atrophy** (Fig. 17.10), which may be preceded by swelling, is a feature of severe compressive optic neuropathy. Important causes include thyroid eye disease and optic nerve tumours.
2. **Opticociliary shunts** consist of enlarged pre-existing parapapillary capillaries which shunt blood from the central retinal venous circulation to the parapapillary choroidal circulation when there is obstruction of the normal drainage channels (Fig. 17.11d). On ophthalmoscopy the vessels appear as large tortuous channels most

Fig. 17.10
Optic atrophy

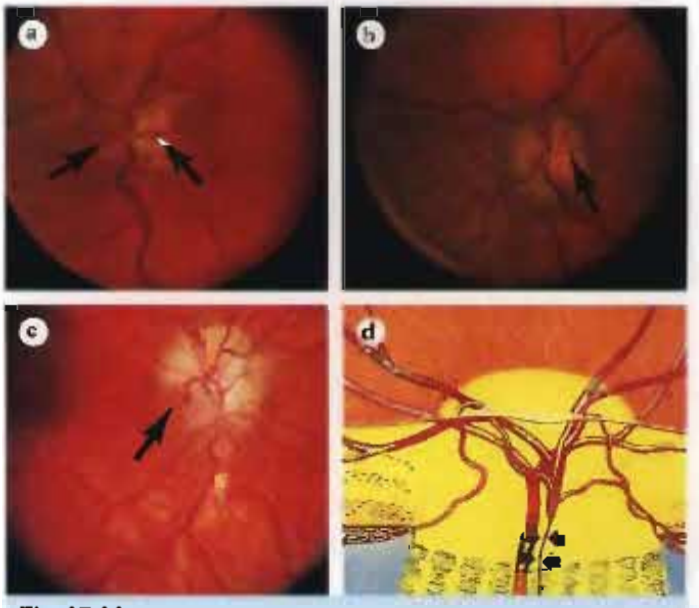


Fig. 17.11
Opticociliary shunts (see text) (Courtesy of Wilmer Institute)

frequently on the temporal side, which disappear at the disc margin (Fig. 17.11a–c). Although rare, they may be associated with any orbital or optic nerve tumour which compresses the intraorbital optic nerve and impairs blood flow through the central retinal vein. The most common tumour associated with shunts is the optic nerve sheath meningioma but may also occur with optic nerve gliomas and cavernous haemangiomas.

Choroidal folds

These are a series of roughly parallel alternating light and dark delicate lines or striae which are most frequently noted at the posterior pole (Fig. 17.12). Choroidal folds may occur in a wide variety of orbital lesions including tumours, dysthyroid ophthalmopathy, inflammatory conditions and mucoceles. The folds are usually asymptomatic and do not cause visual loss although some patients develop an increase in hypermetropia. Although choroidal folds tend to be more common with greater amounts of proptosis and anteriorly located tumours, in some cases their presence can precede the onset of clinically evident proptosis.

Retinal vascular changes

1. **Venous dilatation** and **tortuosity** characteristically occur in orbital arteriovenous communications.
2. **Venous dilatation** may also be associated with disc swelling in patients with an orbital mass.
3. **Vascular occlusions** may occur in carotid–cavernous fistulae, orbital cellulitis and optic nerve tumours.

Special investigations

1. **CT** is useful for depicting bony structures and the location and size of space-occupying lesions. It is of particular value in patients with orbital trauma because it can detect small fractures, foreign bodies, blood, herniation of extraocular muscle and emphysema. It is, however, unable to distinguish different pathological soft tissue masses which are radiologically isodense.
2. **MRI** can image orbital apex lesions and intracranial extension of orbital tumours. Serial short tau inversion recovery (STIR) scans are valuable in assessing inflammatory activity in thyroid eye disease.
3. **Plain radiographs** have diminished in importance since the advent of CT and MRI. The two main views are as follows:
   a. *The Caldwell*, taken with the patient's nose and forehead touching the film, is most useful in detecting orbital lesions (Fig. 17.13).
   b. *The Waters*, taken with the patient's chin slightly elevated, is best in detecting orbital floor fractures (Fig. 17.14).

Fig. 17.13
Caldwell view

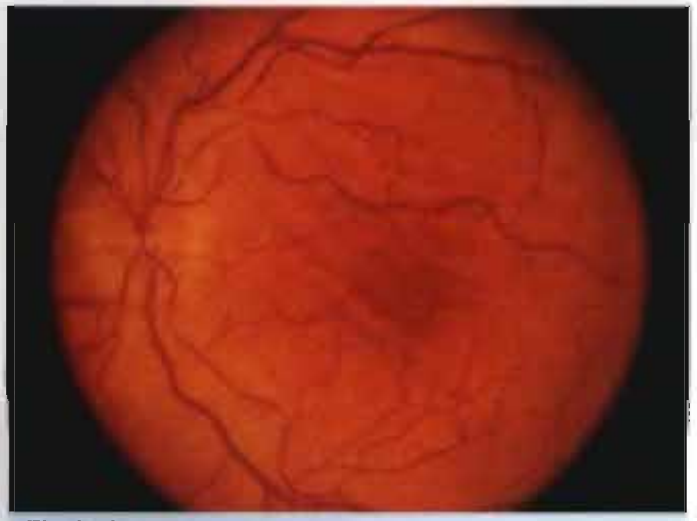


Fig. 17.12
Choroidal folds (Courtesy of C. Barry)

Fig. 17.14
Waters view showing herniation of orbital contents into the maxillary antrum through a blow-out fracture of the orbital floor (arrow)

4. **Fine-needle biopsy** is performed under CT guidance using a 23-gauge needle. This technique is particularly valuable in patients with suspected orbital metastases and in those with secondary orbital invasion by neoplasms from contiguous structures. Potential problems include haemorrhage and ocular penetration.

Thyroid eye disease

Introduction

Thyrotoxicosis

Thyrotoxicosis (Graves disease) is an autoimmune disorder which usually presents in the third to fourth decades of life and affects women more commonly than men (*see* Chapter 20). Thyroid eye disease (TED) may occur in the absence of clinical and biochemical evidence of thyroid dysfunction. More commonly, systemic features are present, but they may follow a different course from TED. The occurrence of signs of Graves disease in a patient who is not clinically hyperthyroid is referred to as euthyroid or ophthalmic Graves disease. This is the form most frequently presenting to ophthalmologists.

Pathogenesis

This involves an organ-specific autoimmune reaction in which a humoral agent (IgG antibody) produces the following changes:

1. **Inflammation of extraocular muscles** characterized by pleomorphic cellular infiltration (Fig. 17.15), associated with increased secretion of glycosaminoglycans and osmotic imbibition of water. The muscles become enlarged, sometimes up to eight times their normal size, and may compress the optic nerve (Fig. 17.16). Subsequent degeneration of muscle fibres eventually leads to fibrosis, which exerts a tethering effect on the involved muscle, resulting in restrictive myopathy and diplopia.
2. **Inflammatory cellular infiltration** with lymphocytes, plasma cells, macrophages and mast cells of the interstitial tissues, orbital fat and lacrimal glands with accumulation of glycosaminoglycans and retention of fluid. This causes increase in the volume of orbital contents and secondary elevation of intraorbital pressure, which may itself cause further fluid retention within the orbit.

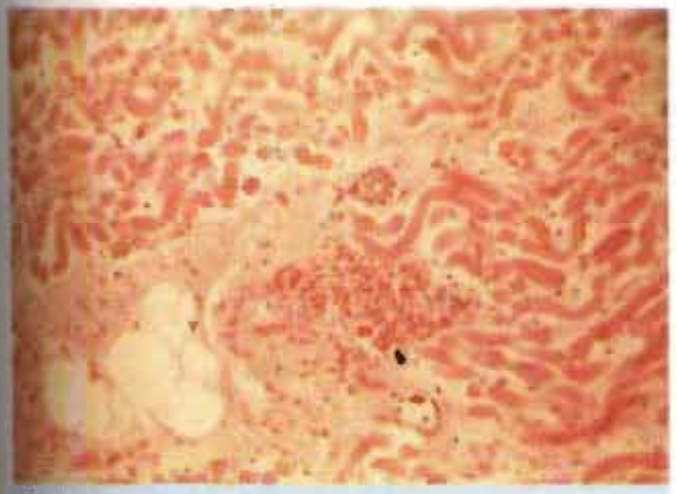


Fig. 17.15
Round cell infiltration of an extraocular muscle in thyroid eye disease

Fig. 17.16
Axial CT scan showing enlarged extraocular muscles in thyroid eye disease

Clinical manifestations

TED may precede, coincide with or follow hyperthyroidism and bears no relationship to the severity of thyroid dysfunction. It may vary from being merely a nuisance, to blindness secondary to exposure keratopathy or optic neuropathy. The five main clinical manifestations of TED are: (a) *soft tissue involvement*, (b) *lid retraction*, (c) *proptosis*, (d) *optic neuropathy* and (e) *restrictive myopathy*. There are two stages in the development of the disease:

1. **Congestive** (inflammatory) stage in which the eyes are red and painful. This tends to remit within 3 years and only 10% of patients develop serious long-term ocular problems.
2. **Fibrotic** (quiescent) stage in which the eyes are white, although a painless motility defect may be present.

Soft tissue involvement

Clinical features

1. **Symptoms** include grittiness, photophobia, lacrimation and retrobulbar discomfort.
2. **Signs**
   a. ***Periorbital and lid swelling*** is caused by oedema and infiltration behind the orbital septum which may be associated with prolapse of retroseptal fat into the eyelids (Fig. 17.17).

b. ***Conjunctival and episcleral hyperaemia*** is a sensitive sign of inflammatory activity. Intense focal hyperaemia may outline the insertions of the horizontal recti (Fig. 17.18).
c. ***Chemosis*** refers to oedema of the conjunctiva and caruncle. If minimal it is manifest as a small fold of redundant conjunctiva overhanging the lower lid margin. In severe cases the conjunctiva prolapses between the lids (Fig. 17.19).
d. ***Superior limbic keratoconjunctivitis*** (Fig. 17.20).
e. ***Keratoconjunctivitis sicca*** secondary to infiltration of the lacrimal glands.

Fig. 17.17
Severe periorbital swelling in thyroid eye disease

Fig. 17.18
Conjunctival and episcleral injection over a horizontal rectus muscle in thyroid eye disease

Fig. 17.19
Severe chemosis in thyroid eye disease

Fig. 17.20
Superior limbic keratoconjunctivitis in thyroid eye disease

Management

1. **Topical lubricants** for superior limbic keratoconjunctivitis corneal exposure and dryness.
2. **Head elevation** with three pillows during sleep to reduce periorbital oedema.
3. **Taping of the eyelids** during sleep may alleviate mild exposure keratopathy.

Lid retraction

Pathogenesis

Retraction of upper and lower lids occurs in about 50% of patients with Graves disease as a result of the following postulated mechanisms:

1. **Fibrotic contracture** of the levator associated with adhesions with the overlying orbital tissues causes lid retraction, worse on downgaze. Fibrosis of the inferior rectus muscle may similarly induce retraction of the lower eyelid via its capsulopalpebral head.
2. **Secondary overaction** of the levator–superior rectus complex in response to hypophoria produced by fibrosis and tethering of the inferior rectus muscle, evidenced by increased lid retraction from downgaze to upgaze. Retraction of the lower eyelid resulting from overaction of the inferior rectus may also occur secondary to fibrosis of the superior rectus muscle.
3. **Humorally induced overaction** of Müller muscle as a result of sympathetic overstimulation secondary to high levels of thyroid hormones. Supporting this hypothesis is the observation that lid retraction may sometimes be lessened by a topical sympatholytic drug (guanethidine); against it is the absence of associated pupillary dilatation and the fact that lid retraction may occur without hyperthyroidism.

Signs

The upper lid margin normally rests 2 mm below the limbus (Fig. 17.21, right eye). Lid retraction is suspected when the

Fig. 17.21
Right eye shows normal lid positions; left eye shows lid retraction and mild proptosis in thyroid eye disease (Courtesy of G. Rose)

Fig. 17.24
Kocher sign in thyroid eye disease

Fig. 17.22
Bilateral lid retraction but no proptosis in thyroid eye disease (Courtesy of G. Rose)

margin is either level with or above the superior limbus, allowing sclera to be visible ('scleral show') (Fig. 17.21, left eye). Likewise, the lower eyelid normally rests at the inferior limbus; retraction is suspected when sclera shows below the limbus. Lid retraction may occur in isolation (Fig. 17.22) or in association with proptosis, which exaggerates its severity.

1. **Dalrymple** sign is lid retraction in primary gaze.
2. **von Graefe** sign signifies retarded descent of the upper lid on downgaze (Fig. 17.23).
3. **Kocher** sign is a staring and frightened appearance of the eyes which is particularly marked on attentive fixation (Fig. 17.24).

Management

Mild lid retraction does not require treatment because it frequently improves spontaneously. Control of hyperthyroidism may also be beneficial. Surgery to decrease the vertical dimensions of the palpebral fissures may be considered in patients with significant but stable lid retraction, but only after addressing proptosis and strabismus. In general, therefore, the sequence of surgical procedures in TED is: (a) *orbit*, (b) *strabismus* and (c) *eyelid*. The rationale for this sequence is that orbital decompression may affect both ocular motility and eyelid position, and extraocular muscle surgery may also influence eyelid position. The main surgical procedures for lid retraction are:

1. **Inferior rectus recession** when inferior rectus fibrosis is thought to be significant.
2. **Müllerotomy** (disinsertion of Müller muscle) for mild lid retraction. More severe cases may also require recession/disinsertion of the levator aponeurosis and the suspensory ligament of the superior conjunctival fornix.
3. **Recession of lower lid retractors** with scleral graft when retraction of the lower lid is 2 mm or more.

Fig. 17.23
von Graefe sign (right eye) in thyroid eye disease

Proptosis

Signs

Proptosis is axial, unilateral or bilateral, symmetrical or asymmetrical, and frequently permanent. Severe proptosis (Fig. 17.25) may compromise lid closure, with resultant exposure keratopathy and corneal ulceration.

Management

This is controversial. Some favour early surgical decompression whereas others consider surgery only when non-invasive methods have failed or are inappropriate.

1. **Systemic steroids** may be used in rapidly progressive and painful proptosis during the congestive phase, unless contraindicated (e.g. tuberculosis or peptic ulceration).
   a. ***Oral prednisolone*** 60–80 mg/day is given initially. Reduction in discomfort, chemosis and periorbital oedema usually occurs within 48 hours, at which point the dose should be tapered. Maximal response is usually achieved within 2–8 weeks. Ideally steroid therapy should be discontinued after about 3 months, although long-term low-dose maintenance may be necessary.
   b. ***Intravenous methylprednisolone*** (0.5 g in 200 ml isotonic saline given over 30 minutes), which may be repeated after 48 hours, may also be effective but is usually reserved for compressive optic neuropathy. This is because of potential cardiovascular risks which mandate supervision by a physician.
2. **Radiotherapy** is an alternative when steroids are contraindicated or ineffective. A positive response is usually evident within 6 weeks, with maximal improvement by 4 months.
3. **Combined therapy** with irradiation, azathioprine and low-dose prednisolone may be more effective than steroids or radiotherapy alone.
4. **Surgical decompression** may be considered either as primary treatment or when non-invasive methods are ineffective, such as for cosmetically unacceptable proptosis in the quiescent phase. Decompression, which is often performed endoscopically, may involve the following:
   a. ***Two-wall*** (antral–ethmoidal) involves removal of a part of the floor and the posterior portion of the medial wall (Fig. 17.26). This affords 3–6 mm of retroplacement of the globe.
   b. ***Three-wall*** involves an antral–ethmoidal decompression and removal of the lateral wall. The amount of retroplacement achieved is 6–10 mm.
   c. ***Four-wall*** involves a three-wall decompression, removal of the lateral half of the orbital roof and a large portion of the sphenoid at the apex of the orbit. This affords 10–16 mm of retroplacement and is reserved for very severe proptosis.

Optic neuropathy

Optic neuropathy is a serious complication affecting about 5% of patients. It is caused by compression of the optic nerve or its blood supply at the orbital apex by the congested and enlarged recti. Such compression, which may occur in the absence of significant proptosis, may lead to severe permanent, but preventable visual impairment.

Clinical features

1. **Presentation** is with impairment of central vision. In order to detect early involvement, patients should be advised to monitor their own visual function by alternatively occluding each eye and reading small print and assessing the intensity of colours, for example, on a television screen.
2. **Signs**
   - Visual acuity is usually reduced, but not invariably, and is associated with a relative afferent pupillary defect, colour desaturation and diminished light brightness appreciation.
   - Visual field defects may be central or paracentral and may be combined with nerve fibre bundle defects. These

Fig. 17.25
Severe bilateral proptosis and lid retraction in thyroid eye disease (Courtesy of G. Rose)

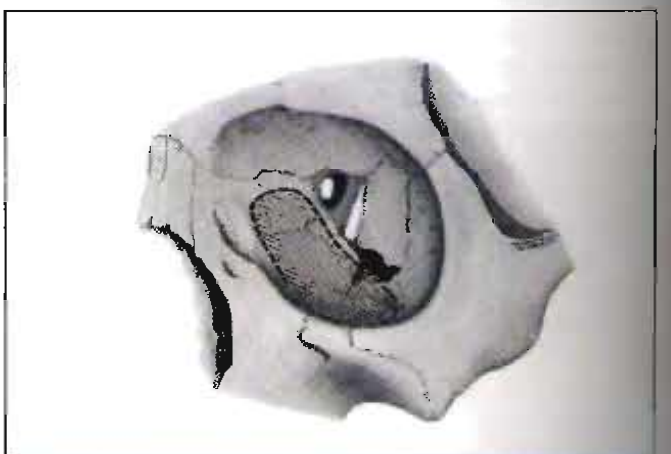


Fig. 17.26
Two-wall orbital decompression

findings, combined with elevated intraocular pressure, may be confused with primary open-angle glaucoma (*see* below).
- The optic disc is usually normal, occasionally swollen and rarely atrophic.

> ***NB:*** It is important not to attribute disproportionate visual loss to minor corneal complications and miss optic neuropathy.

Treatment

Initial treatment is usually with intravenous methylprednisolone. Orbital decompression may be considered if this is ineffective or inappropriate.

Restrictive myopathy

Signs

Between 30% and 50% of patients with TED develop ophthalmoplegia which may be permanent. Ocular motility is restricted initially by inflammatory oedema and later by fibrosis. Intraocular pressure may increase in upgaze due to ocular compresston by a fibrotic inferior rectus. Occasionally, there may be a sustained tncrease in the intraocular pressure through compression of the globe by a combination of fibrotic extraocular muscles and increased intraorbital pressure. In order of frequency the four ocular motility defects are:

1. **Elevation** defect caused by fibrotic contracture of the inferior rectus (Fig. 17.27), which may mimic a superior rectus palsy.
2. **Abduction** defect due to fibrosis of the medial rectus (Fig. 17.28), which may simulate sixth nerve palsy.
3. **Depression** defect secondary to fibrosis of the superior rectus.
4. **Adduction** defect caused by fibrosis of the lateral rectus.

Fig. 17.27
Restricted left elevation due to a tight left inferior rectus in thyroid eye disease

Fig. 17.28
Restricted left abduction due to a tight left medial rectus in thyroid eye disease

Management

1. **Surgery**
   - *a.* ***The indication*** is diplopia in the primary or reading positions of gaze, provided the disease is quiescent and the angle of deviation has been stable for at least 6 months. Until these criteria are met diplopia may be alleviated, if possible, with prisms.
   - *b.* ***The goal*** is to achieve binocular single vision in the primary and reading positions. Restrictive myopathy, which causes incomitant strabismus, often precludes binocularity in all positions of gaze. However, with time the field of binocular single vision may enlarge as a result of increasing vergences.
   - *c.* ***The technique*** most commonly involves recession of the inferior and/or medial recti, for best results on adjustable sutures. The suture is adjusted on the first postoperative day to obtain optimal alignment, and the patient is encouraged to practise achieving single vision with a distant target such as a television.
2. **Botulinum toxin injection** into the involved muscle may be useful in selected cases.

Infections

Preseptal cellulitis

Preseptal cellulitis is an infection of the subcutaneous tissues anterior to the orbital septum. Although not strictly an orbital disease, it is included hereunder because it must be differentiated from the much less common but potentially more serious orbital cellulitis. Occasionally rapid progression to orbital cellulitis may occur.

1. **Causes**
   - *a.* ***Skin trauma*** such as laceration or insect bites. The offending organism is usually *Staph. aureus* or *Strep. pyogenes*.
   - *b.* ***Spread of local infection***, such as from an acute hordeolum or dacryocystitis.
   - *c.* ***From remote infection*** of the upper respiratory tract or middle ear by haematogenous spread.
2. **Signs.** Unilateral, tender, and red periorbital and lid oedema (Fig. 17.29).

Fig. 17.29
Preseptal cellulitis due to a skin laceration

Fig. 17.30
Sinus-related orbital cellulitis

NB: Unlike orbital cellulitis proptosis is absent. Visual acuity, pupillary reactions and ocular motility are unimpaired.

3. **Treatment** is with oral co-amoxiclav 250 mg every 6 hours. Very severe infection may require intramuscular benzylpenicillin 2.4–4.8 mg in four divided doses and oral flucloxacillin 250–500 mg every 6 hours.

Bacterial orbital cellulitis

Bacterial orbital cellulitis is a life-threatening infection of the soft tissues behind the orbital septum. It can occur at any age but is more common in children. The most frequent causative organisms are *Strep. pneumoniae, Staph. aureus, Strep. pyogenes* and *H. influenzae.*

Causes

1. **Sinus-related**, most commonly ethmoidal, typically affects children and young adults.
2. **Extension of preseptal cellulitis** through the orbital septum.
3. **Local spread** from adjacent dacryocystitis, and mid-facial or dental infection. The last condition may cause orbital cellulitis via an intermediary maxillary sinusitis.
4. **Haematogenous spread.**
5. **Post-traumatic** develops within 72 hours of an injury that penetrates the orbital septum. The typical clinical features may be masked by associated laceration or haematoma.
6. **Post-surgical** may complicate retinal, lacrimal or orbital surgery.

Clinical features

1. **Presentation** is with a rapid onset of severe malaise, fever, pain and visual impairment.
2. **Signs**
   - Unilateral, tender, warm and red periorbital and lid oedema (Figs 17.30 and 17.31).

Fig. 17.31
Orbital cellulitis following retinal detachment surgery

   - Proptosis, which is often obscured by lid swelling, is most frequently lateral and downwards.
   - Painful ophthalmoplegia.
   - Optic nerve dysfunction.

Complications

1. **Ocular** complications include exposure keratopathy, raised intraocular pressure, occlusion of the central retinal artery or vein, endophthalmitis and optic neuropathy.
2. **Intracranial** complications, which are rare, include meningitis, brain abscess and cavernous sinus thrombosis. The last is a rare but extremely serious complication which should be suspected when there is evidence of bilateral involvement, rapidly progressive proptosis and congestion of the facial, conjunctival and retinal veins. Additional features include abrupt progression of all clinical signs associated with prostration, severe headache, nausea and vomiting.
3. **Subperiosteal abscess** is most frequently located along the medial orbital wall. It is a serious problem because of the potential for rapid progression and intracranial extension.

Fig. 17.32
Discharging orbital abscess

Fig. 17.33
Axial CT scan showing left preseptal cellulitis

4. **Orbital abscess** is relatively rare in sinus-related orbital cellulitis but may occur in post-traumatic or postoperative cases (Fig. 17.32).

Management

1. **Hospital admission** with frequent ophthalmic and otolaryngological assessment is mandatory. Intracranial abscess formation may necessitate neurosurgical drainage.
2. **Antibiotic therapy** involves intramuscular ceftazidime 1 g every 8 hours and oral metronidazole 500 mg every 8 hours to cover anaerobes. Intravenous vancomycin is a useful alternative in the context of penicillin allergy. Antibiotic therapy should be continued until the patient is apyrexial for 4 days.
3. **Optic nerve function** should be monitored every 4 hours by testing pupillary reactions, visual acuity, colour vision and light brightness appreciation.
4. **Investigations**, where appropriate, include the following:
   - White cell count.
   - Blood culture.
   - CT of the orbit, sinuses and brain. Orbital CT is useful in the differentiation between severe preseptal cellulitis and orbital cellulitis (Fig. 17.33).
   - Lumbar puncture if meningeal or cerebral signs develop.
5. **Surgical intervention** should be considered in the following circumstances:
   - Unresponsiveness to antibiotics.
   - Decreasing vision.
   - Orbital or subperiosteal abscess.
   - Atypical picture, which may merit diagnostic biopsy.

> ***NB:*** It is usually necessary to drain the infected sinuses as well as the orbit.

Rhino-orbital mucormycosis

Mucormycosis is a rare opportunistic infection caused by fungi of the family *Mucoraceae*, which typically affects patients with diabetic ketoacidosis or immunosuppression. This aggressive and fatal infection is acquired by the inhalation of spores, which give rise to an upper respiratory infection. The infection then spreads to the contiguous sinuses and subsequently to the orbit and brain. Invasion of blood vessels by the hyphae results in occlusive vasculitis with ischaemic infarction of orbital tissues.

1. **Presentation** is with gradual-onset facial and periorbital swelling, diplopia and visual loss.
2. **Signs**
   - Ischaemic infarction superimposed on septic necrosis is responsible for the black eschar which may develop on the palate, turbinates, nasal septum, skin and eyelids (Fig. 17.34).
   - Ophthalmoplegia.
   - Progression is slower than in bacterial orbital cellulitis.
3. **Complications** include retinal vascular occlusion, multiple cranial nerve palsies and cerebrovascular occlusion.

Fig. 17.34
Necrosis of the eyelid in rhino-orbital mucormycosis

4. **Treatment**
   - Intravenous amphotericin.
   - Daily packing and irrigation of the involved areas with amphotericin.
   - Wide excision of devitalized and necrotic tissues.
   - Adjunctive hyperbaric oxygen may be helpful.
   - Correction of the underlying metabolic defect, if possible.
   - Exenteration may be required in severe unresponsive cases.

Inflammatory disease

Idiopathic orbital inflammatory disease

Idiopathic orbital inflammatory disease (IOID), previously referred to as orbital pseudo-tumour, is an uncommon disorder characterized by non-neoplastic, non-infectious, space-occupying, orbital lesions. The inflammatory process may involve any or all of the orbital soft tissues. Histopathological analysis reveals pleomorphic cellular inflammatory infiltration followed by reactive fibrosis, but has thus far shown no correlation between clinicopathological features and the subsequent course of the disease. Unilateral disease is the rule in adults, although in children bilateral involvement may occur. Simultaneous orbital and sinus involvement is a rare distinct entity.

Clinical features

1. **Presentation** is in the third to sixth decades with acute redness, swelling and pain, which is usually unilateral.
2. **Signs**
   - Congestive proptosis and ophthalmoplegia.
   - Optic nerve dysfunction if the inflammation involves the posterior orbit.
3. **Course.** This follows one of the following patterns:
   - Spontaneous remission after a few weeks without sequelae.
   - Prolonged intermittent episodes of activity with no eventual remission.
   - Severe prolonged inflammation eventually leading to progressive fibrosis of orbital tissues, resulting in a 'frozen orbit' characterized by ophthalmoplegia (Fig. 17.35a–c), which may be associated with ptosis and visual impairment caused by optic nerve involvement.

Management

1. **Observation**, for relatively mild disease, in anticipation of spontaneous remission.
2. **Biopsy** may be required in persistent cases to confirm the diagnosis and to rule out neoplasia.
3. **Systemic steroids** are effective in 50–75% of patients with moderate to severe involvement. Oral prednisolone, initially 60–80 mg/day, is later tapered and discontinued, depending on clinical response, although it may need to be reintroduced in the event of recurrence.
4. **Radiotherapy** may be considered if there has been no improvement after 2 weeks of adequate steroid therapy. Even a low-dose treatment (i.e. 10 Gy) may produce long-term, and sometimes permanent, remission.
5. **Cytotoxic drugs** such as cyclophosphamide 200 mg/day may be necessary in the context of resistance to both steroids and radiotherapy.

Fig. 17.35
Ophthalmoplegia due to a 'frozen orbit' (Courtesy of G. Rose)

Differential diagnosis

1. **Bacterial orbital cellulitis** should be considered when the anterior orbital tissues are markedly inflamed. A trial of systemic antibiotics may be necessary before the correct diagnosis becomes apparent.
2. **Severe acute TED** shares many features with IOID, but is commonly bilateral, while IOID is usually unilateral.
3. **Systemic disorders** such as Wegener granulomatosis, polyarteritis nodosa and Waldenström macroglobulinaemia may manifest orbital involvement similar to IOID.
4. **Malignant orbital tumours**, particularly metastatic.
5. **Ruptured dermoid cyst** may evoke a secondary painful granulomatous inflammatory reaction.

Acute dacryoadenitis

Lacrimal gland involvement occurs in about 25% of patients with IOID. More commonly, however, dacryoadenitis occurs in isolation, resolves spontaneously and does not require treatment.

Clinical features

1. **Presentation** is with acute discomfort in the region of the lacrimal gland.
2. **Signs**
   - Swelling of the lateral aspect of the eyelid giving rise to a characteristic S-shaped ptosis and mild downward and inward dystopia (Fig. 17.36).
   - Tenderness over the lacrimal gland fossa.
   - Injection of the palpebral portion of the lacrimal gland and adjacent conjunctiva (Fig. 17.37).
   - Lacrimal secretion may be reduced.

Differential diagnosis

1. **Lacrimal gland infection** caused by mumps, mononucleosis and, less commonly, bacteria.
2. **Ruptured dermoid cyst** may cause localized inflammation in the region of the lacrimal gland.

Fig. 17.36
Acute right dacryoadenitis (Courtesy of G. Rose)

Fig. 17.37
Injection of the lacrimal gland and adjacent conjunctiva in acute dacryoadenitis

3. **Malignant lacrimal gland tumours** may cause pain but the onset is not usually acute.

Orbital myositis

This idiopathic, non-specific inflammation of one or more extraocular muscles is considered a subtype of IOID.

Clinical features

1. **Presentation** is usually in early adult life with acute pain exacerbated by eye movements and diplopia.
2. **Signs**
   - Lid oedema, ptosis and chemosis.
   - Worsening of pain on attempted gaze into the field of action of the involved muscle(s), usually associated with diplopia due to underaction.
   - Vascular injection over the involved muscle.
   - Mild proptosis.
3. **CT** shows fusiform enlargement of the affected muscles, with or without involvement of the tendons of insertion (Fig. 17.38).
4. **Differential diagnosis** includes orbital cellulitis, dysthyroid myopathy and Tolosa–Hunt syndrome.

Fig. 17.38
Axial CT scan showing fusiform enlargement of the left lateral rectus muscle in orbital myositis

5. **Course**
   a. *Acute non-recurrent* involvement which resolves spontaneously within 6 weeks.
   b. *Chronic* disease characterized by either a single episode persisting for longer than 2 months (often for years) or recurrent attacks that may result in permanent restrictive myopathy.

Treatment

This is aimed at relieving discomfort and dysfunction, shortening the course and preventing recurrences.

1. **NSAIDs** may be adequate in mild disease.
2. **Systemic steroids** are generally required and usually produce dramatic improvement, although recurrences occur in 50% of cases.
3. **Radiotherapy** is also effective, particularly in limiting recurrence.

Tolosa–Hunt syndrome

This rare condition is caused by non-specific granulomatous inflammation of the cavernous sinus, superior orbital fissure and/or orbital apex. The clinical course is characterized by remissions and recurrences.

1. **Presentation** is with diplopia associated with ipsilateral periorbital or hemicranial pain.
2. **Signs**
   - Proptosis, if present, is usually mild.
   - Ocular motor nerve palsies often with involvement of the pupil.
   - Sensory loss along the distribution of the first and second divisions of the trigeminal nerve.
3. **Treatment** is with systemic steroids.

Wegener granulomatosis

Wegener granulomatosis (*see* Chapter 20) involves the orbit, often bilaterally, usually by contiguous spread from the paranasal sinuses or nasopharynx. Primary orbital involvement is less common. The possibility of Wegener granulomatosis should be considered in any patient with bilateral orbital inflammation, particularly if associated with sinus pathology. The antineutrophilic cytoplasmic antibody (cANCA) is a very useful serological test.

1. **Signs**
   - Proptosis, orbital congestion and ophthalmoplegia (often bilateral).
   - Dacryoadenitis and nasolacrimal duct obstruction.
   - Coexistent manifestations include scleritis and peripheral ulcerative keratitis.
2. **Treatment**
   - Systemic cyclophosphamide and steroids are highly effective. In resistant cases cyclosporin, azathioprine, antithymocyte globulin or plasmapheresis may be useful.
   - Surgical orbital decompression may be required for severe orbital involvement.

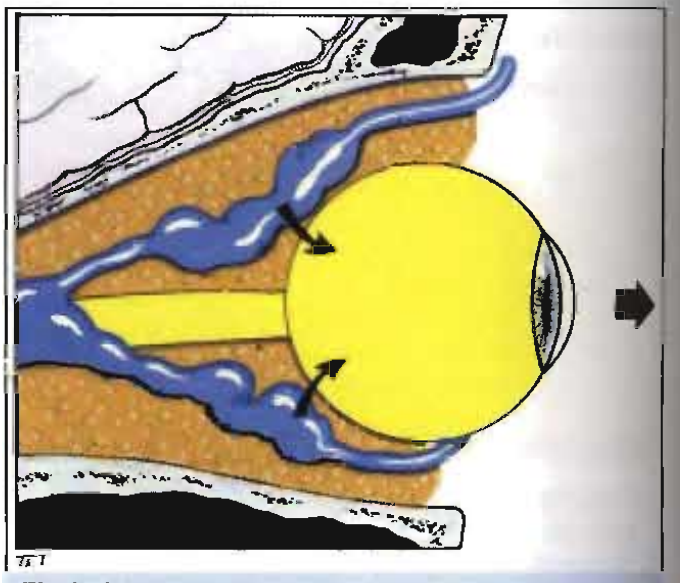


Fig. 17.39
Mechanism of intermittent proptosis caused by orbital varices

Fig. 17.40
Orbital varices.
(a) Before Valsalva manoeuvre;
(b) with Valsalva manoeuvre

Vascular malformations

Primary varices

Primary varices consist of weakened segments of the orbital venous system, of variable length and complexity. Intrinsic to the circulation, they enlarge with increased venous pressure, their distensibility varying with the residual thickness and strength of their walls (Fig. 17.39). Most cases are unilateral and the most frequent site is upper nasal. CT and plain radiographs show phleboliths in about 20% of cases.

1. **Presentation** ranges from early childhood to late middle age.
2. **Signs**
   a. ***Intermittent proptosis*** without external signs. The proptosis is non-pulsatile and is not associated with a bruit. As the orbital veins are devoid of valves, rapidly reversible proptosis may be precipitated or accentuated by increasing venous pressure through coughing, straining, Valsalva manoeuvre (Fig. 17.40), assuming the dependent position or external compression of the jugular veins. Patients with long-standing lesions may develop atrophy of surrounding fat and enophthalmos associated with a deepened superior sulcus in the resting position, reversible with increase in venous pressure.
   b. ***Visible lesions*** in the eyelid (Fig. 17.41) and under the conjunctiva (Fig. 17.42), which may also be accentuated by performing the Valsalva manoeuvre.
   c. ***A combination*** of visible lesions and proptosis (the most common).
3. **Complications** include acute haemorrhage and thrombosis.
4. **Treatment** by surgical excision is technically difficult and often incomplete because the lesions are friable and bleed easily. Indications include recurrent thrombosis, pain, severe proptosis and optic nerve compression.

Fig. 17.42
Orbital varices extending under the conjunctiva

Lymphangioma

Lymphangiomas are not neoplasms but abortive, non-functional, benign vascular malformations that arborize through the orbit and may also involve the oropharynx. Although haemodynamically isolated from the circulation, bleeding into the lumen may occur with resultant blood-filled 'chocolate' cysts. Lymphangiomas may be confused with orbital venous anomalies and haemangiomas.

1. **Presentation** is usually in early childhood.
2. **Signs**
   a. ***Anterior lesions*** typically manifest several soft bluish masses in the upper nasal quadrant with an associated cystic conjunctival component.
   b. ***Posterior lesions*** may cause slowly progressive proptosis, or initially may lie dormant and later present with sudden painful proptosis secondary to spontaneous haemorrhage. The blood subsequently becomes encysted with the formation of 'chocolate cysts' which may regress spontaneously with time.
3. **Treatment** by surgical excision is difficult because lymphangiomas are friable, not encapsulated, bleed easily and may infiltrate normal orbital tissues. Persistent sight-threatening 'chocolate cysts' should be drained or removed subtotally by controlled vaporization using a carbon dioxide laser.

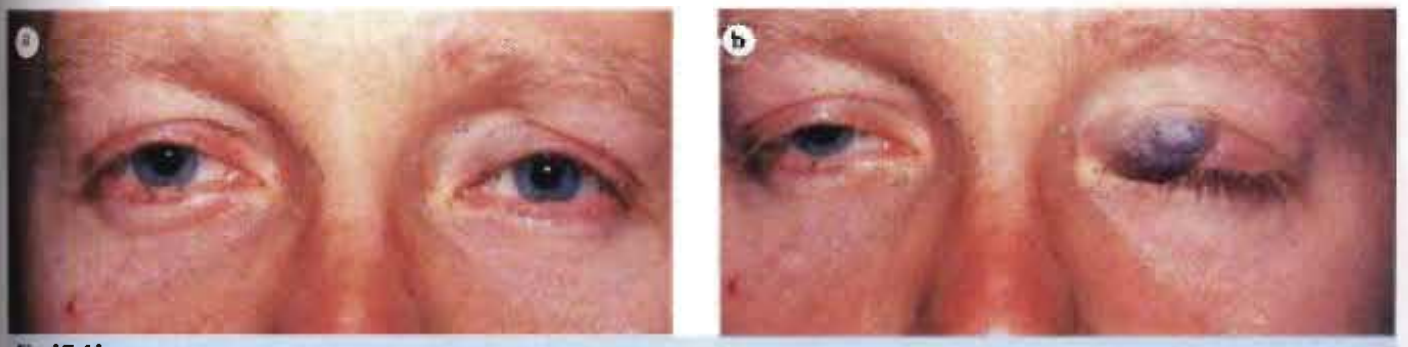


Fig. 17.41
Orbital varices involving the left eyelid. (a) Before Valsalva manoeuvre; (b) with Valsalva manoeuvre (Courtesy of G. Rose)

Carotid–cavernous fistula

An arteriovenous fistula is an abnormal communication between an artery and a vein. The blood within the affected vein becomes 'arterialized', the venous pressure rises, and venous drainage may be altered in both rate and direction. The arterial pressure and perfusion are also reduced. A carotid–cavernous fistula is one such communication between the carotid artery and the cavernous sinus. When arterial blood flows anteriorly into the ophthalmic veins, ocular manifestations occur because of venous and arterial stasis around the eye and orbit, increased episcleral venous pressure and decrease in arterial blood flow to the cranial nerves within the cavernous sinus. Carotid–cavernous fistulae can be classified on the basis of: (a) *aetiology* (spontaneous and traumatic), (b) *haemodynamics* (high and low flow) and (c) *anatomy* (direct and indirect).

Fig. 17.43
Chemosis in a high-flow carotid–cavernous fistula

Direct carotid–cavernous fistula

Representing 70–90% of all cases, direct fistulae are high-flow shunts in which carotid artery blood passes directly into the cavernous sinus through a defect in the wall of the intracavernous portion of the internal carotid artery as a result of the following:

1. **Trauma** is responsible for 75% of cases. A basal skull fracture may cause a tear in the intracavernous internal carotid artery with sudden and dramatic onset of symptoms and signs.
2. **Spontaneous rupture** of an intracavernous carotid aneurysm or an atherosclerotic artery accounts for the remainder. Post-menopausal hypertensive women are at particular risk. Spontaneous fistulae usually have lower flow rates and less severe symptoms than traumatic fistulae.

Clinical features

1. **Presentation** may be days or weeks after head injury with the classic triad of pulsatile proptosis, conjunctival chemosis and a flushing noise in the head.
2. **Signs** are usually ipsilateral to the fistula but may be bilateral or even contralateral because of the vascular connections across the midline between the two cavernous sinuses.
   a. Anterior
   - Ptosis and chemosis (Fig. 17.43).
   - Pulsatile proptosis associated with a bruit and a thrill, both of which can be abolished by ipsilateral carotid compression in the neck. A cephalic bruit may also be present.
   - Increased intraocular pressure from elevated episcleral venous pressure and orbital congestion.
   - Anterior segment ischaemia characterized by corneal epithelial oedema, aqueous cells and flare, iris atrophy, cataract and rubeosis iridis.

   *b. **Ophthalmoplegia*** occurs in 60–70% of cases due to ocular motor nerve damage by the initial trauma, the intracavernous carotid aneurysm or by the fistula itself. The sixth nerve is most frequently affected because of its free location within the cavernous sinus. The third and fourth nerves, situated in the lateral wall of the sinus, are less frequently involved. Engorgement and swelling of extraocular muscles may also contribute to defective ocular motility.
   *c. **Fundus*** examination shows optic disc swelling, venous dilatation and intraretinal haemorrhages from venous stasis and impaired retinal blood flow. Preretinal or vitreous haemorrhages are rare.
3. **Special investigations.** CT and MRI will show prominence of the superior ophthalmic vein and diffuse enlargement of extraocular muscles. Definitive diagnosis involves arterial angiography with selective injection of both internal and external carotid arteries, and the vertebral circulation.
4. **Visual prognosis** is poor, about 90% of patients developing severe visual loss.
   *a. **Immediate*** visual loss may be due to coincidental ocular or optic nerve damage at the time of head trauma.
   *b. **Delayed*** visual loss may be due to a variety of complications such as exposure keratopathy, secondary glaucoma, central retinal vein occlusion, anterior segment ischaemia or ischaemic optic neuropathy.

Treatment

Most carotid–cavernous fistulae are not life-threatening; the major organ at risk is the eye. Surgery is indicated if spontaneous closure secondary to thrombosis of the cavernous sinus does not occur. A post-traumatic fistula is much less likely to close on its own than a spontaneous fistula because of higher blood flow.

1. **Indications** for treatment are secondary glaucoma, diplopia, intolerable bruit or headache, severe proptosis

causing exposure keratopathy and anterior segment ischaemia.

2. **Interventional radiology** involves detachable balloon occlusion of the fistula. The balloon is introduced into the cavernous sinus either by an arterial route, through the tear in the internal carotid artery, or by a venous route, through the inferior petrosal sinus or the superior ophthalmic vein.

Indirect carotid–cavernous fistula

In an indirect carotid–cavernous fistula (dural shunt), the intracavernous portion of the internal carotid artery remains intact. Arterial blood flows through the meningeal branches of the external or internal carotid arteries indirectly into the cavernous sinus. Due to slow blood flow, the clinical features are more subtle than in a direct fistula. The condition may therefore be misdiagnosed or missed altogether.

1. **Types**
   - Between meningeal branches of the internal carotid artery and the cavernous sinus.
   - Between meningeal branches of the external carotid artery and the cavernous sinus.
   - Between meningeal branches of both the external and internal carotid arteries and the cavernous sinus.
2. **Causes**
   a. ***Congenital malformations***, in which the onset of symptoms is precipitated by intracranial vascular thrombosis.
   b. ***Spontaneous rupture***, which may be precipitated by minor trauma or straining, especially in hypertensive patients.
3. **Presentation** is with gradual onset of redness of one or both eyes caused by conjunctival vascular engorgement.
4. **Signs** are variable.
   - Dilated conjunctival and episcleral vessels (Fig. 17.44).
   - Exaggerated ocular pulsation best detected on applanation tonometry.
   - Raised intraocular pressure.
   - Mild proptosis occasionally associated with a soft bruit.
   - Ophthalmoplegia most frequently caused by a sixth nerve palsy.
   - Fundus may be normal or manifest moderate venous dilatation.
5. **Differential diagnosis** includes chronic conjunctivitis, thyroid eye disease, glaucoma caused by some other pathology and orbital arteriovenous malformations which may mimic dural shunts.
6. **Treatment** involving 'interventional radiology' to occlude the feeding arteries is often required although some patients recover spontaneously.

Cystic lesions

Dacryops

A dacryops is a ductal cyst of the lacrimal gland. It is the most common orbital cystic lesion and is frequently bilateral.

1. **Signs**. A round, cystic lesion originating from the palpebral portion of the lacrimal gland which protrudes into the superior fornix (Fig. 17.45).
2. **Treatment** is by simple aspiration.

Dermoid cyst

A dermoid cyst is a benign cystic teratoma (choristoma) derived from displacement of ectoderm to a subcutaneous location along embryonic lines of closure. Dermoids are lined by keratinized stratified squamous epithelium (like skin), have a fibrous wall and contain dermal appendages such as sweat glands, sebaceous glands and hair follicles. Epidermoid cysts do not contain such adnexal structures. Dermoids may be (a) *superficial* or (b) *deep*, located anterior or posterior to the orbital septum respectively.

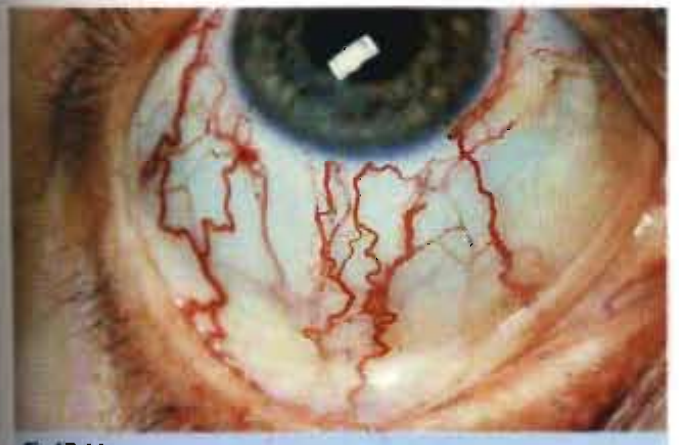


Fig.17.44
Dilated conjunctival and episcleral vessels in a low-flow carotid–cavernous fistula (Courtesy of K. Sehmi)

Fig. 17.45
Dacryops of the lacrimal gland

Superficial dermoid cyst

1. **Presentation** is in infancy with a painless nodule most commonly located in the superotemporal and occasionally the superonasal part of the orbit.
2. **Signs**. A firm, round, smooth, non-tender mass 1–2 cm in diameter which is freely mobile under the skin (Fig. 17.46). The posterior margins are easily palpable, denoting lack of deeper origin or extension.
3. **Treatment** is by excision *in toto*, taking care not to rupture the lesion, since leaking of keratin into the surrounding tissue results in severe granulomatous inflammation.

Fig. 17.46
Superficial dermoid

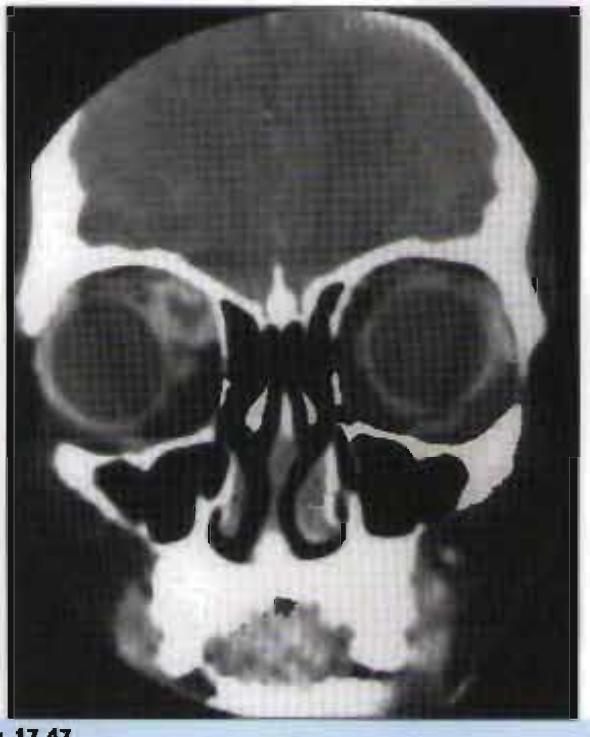


Fig. 17.47
Coronal CT scan showing a deep dermoid in the right medial orbit

Deep dermoid cyst

1. **Presentation** is in adolescence or adult life.
2. **Signs**. Proptosis, dystopia or a mass lesion with indistinct posterior margins. Some deep dermoids, associated with bony defects, may extend into the infratemporal fossa or intracranially.
3. **CT** shows a heterogeneous, well-circumscribed lesion (Fig. 17.47).
4. **Treatment** by excision *in toto* is advisable because deep dermoids enlarge and may leak their contents into adjacent tissues. This induces a painful granulomatous inflammation, often followed by fibrosis. If incompletely excised, they may recur and cause persistent low-grade inflammation.

Mucocele

A mucocele develops when the drainage of normal paranasal sinus secretions is obstructed due to infection, allergy, trauma, tumour or congenital narrowing. A slowly expanding cystic accumulation of mucoid secretions and epithelial debris develops and gradually erodes the bony walls of the sinuses, causing symptoms by encroaching upon surrounding tissues. Orbital invasion occurs usually from frontal or ethmoidal mucoceles, and rarely from those arising in the maxillary sinus.

1. **Presentation** is in adult life with proptosis, dystopia, diplopia or epiphora. Pain is uncommon unless secondary infection develops (mucopyocele).
2. **Signs**. Frontal tenderness, proptosis or dystopia (Fig. 17.48), and periorbital or upper lid swelling (Fig. 17.49).
3. **CT** shows a soft tissue mass with thinning of the bony walls of the sinus.
4. **Treatment** involves complete removal of the mucocele with re-establishment of normal sinus drainage or obliteration of the sinus cavity.

Encephalocele

An encephalocele is formed by herniation of intracranial contents through a congenital defect of the base of the

Fig. 17.48
Left dystopia due to a frontal mucocele

skull. A meningocele contains only dura, while a meningoencephalocele also contains brain tissue. Orbital encephalocele may be (a) *anterior* (fronto-ethmoidal) or (b) *posterior* (associated with dysplasia of the sphenoid bone).

1. **Presentation** is usually during infancy.
2. **Signs**
   - Anterior encephaloceles involve the superomedial part of the orbit and displace the globe forwards and laterally (Fig. 17.50). Posterior encephaloceles displace the globe forwards and downwards.
   - The cyst increases in size on straining or crying and may be reduced by manual pressure.
   - Pulsating proptosis may occur due to communication with the subarachnoid space but, because the communication is not vascular, there is neither a thrill nor a bruit (Fig. 17.51).
3. **CT** shows the bony defect responsible for the herniation.
4. **Differential diagnosis**
   a. *Of anterior* encephaloceles includes other causes of medial canthal swellings such as dermoid cysts and amniontoceles of the lacrimal sac (*see* Fig. 2.24).
   b. *Of posterior* encephaloceles includes other orbital lesions that present during early life such as capillary haemangioma, juvenile xanthogranuloma, teratoma and microphthalmos with cyst.
5. **Associations**
   a. ***Other bony abnormalities*** such as hypertelorism, broad nasal bridge and cleft palate.
   b. ***Ocular associations*** include microphthalmos, colobomas and the morning glory syndrome.
   c. *Neurofibromatosis-1* is frequently associated with posterior encephalocele.

Fig. 17.49
Swelling in the upper eyelid due to a frontal mucocele
(Courtesy of C. Barry)

Fig. 17.50
Anterior encephalocele

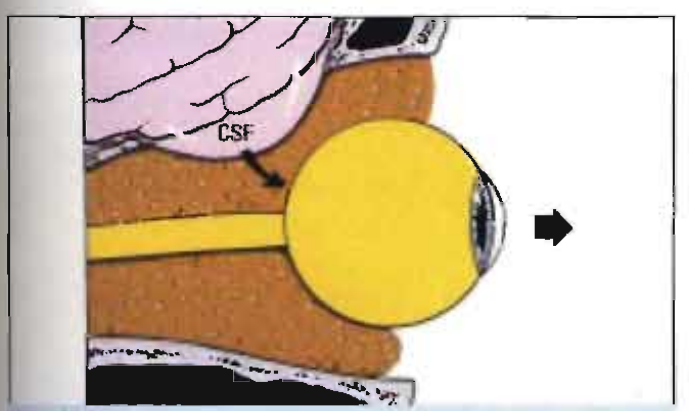


Fig. 17.51
Mechanism of pulsatile proptosis in an encephalocele

Tumours

Capillary haemangioma

The capillary haemangioma is the most common tumour of the orbit and periorbital areas in childhood. This hamartoma may present as a small isolated lesion of minimal clinical significance or as a large disfiguring mass that can cause visual impairment and systemic complications.

Fig. 17.52
Subcutaneous capillary haemangioma and a cutaneous strawberry naevus

Clinical features

The diagnosis can usually be made on inspection alone. The lesions may be superficial, subcutaneous, deep or in combination with various appearances and ocular effects.

1. **Presentation** is usually in the perinatal period, but never at birth.
2. **Signs**
   - Superficial 'strawberry' naevus on the eyelids is common.
   - Subcutaneous haemangioma in the eyelids or superficial orbit that appears dark blue or purple through the overlying skin (Fig. 17.52).
   - The superior anterior orbit is most commonly involved and the tumour may cause dystopia (Fig. 17.53).
   - Deep orbital tumour which gives rise to unilateral proptosis without skin discoloration.
   - Haemangiomatous involvement of the palpebral or forniceal conjunctiva is common and may be an important diagnostic clue.

Fig. 17.53
Early anterior orbital capillary haemangioma

Fig. 17.54
The same patient several months later showing enlargement of the haemangioma

   - A large tumour may enlarge and change in colour to a deep blue during crying or straining, but both pulsation and a bruit are absent.
   - Coexisting capillary haemangiomas on other parts of the body are present in about 25% of cases.
3. **CT** may be required for deep lesions when the diagnosis is not apparent on inspection. The lesion appears as a homogeneous soft tissue mass in the anterior orbit or as an extraconal mass with 'finger-like' posterior expansions. The orbital cavity may show enlargement but there is no bony erosion.
4. **Course.** This is characterized by growth until the age of 1 year (Fig. 17.54) followed by gradual spontaneous involution starting at about 2 years. Complete resolution occurs in 40% by the age of 4 years and 70% by 7 years.

Systemic associations

Children with large haemangiomas may have the following conditions:

1. **High-output heart failure.**
2. **Kasabach–Merritt syndrome**, characterized by thrombocytopenia, anaemia and low levels of coagulant factors.
3. **Maffucl syndrome**, characterized by skin haemangiomas, enchondromata of hands, feet and long bones as well as bowing of long bones.

Treatment

1. **Indications**
   - Amblyopia, most commonly secondary to induced astigmatism and anisometropia.
   - Optic nerve compression.
   - Exposure keratopathy.
   - A severe cosmetic blemish, necrosis or infection.
2. **Methods**
   a. ***Steroid injection*** (triamcinolone acetonide 40 mg combined with betamethasone 6 mg) into the lesion, if subcutaneous, is very effective during the early active stage. Potential complications include retrograde forcing of the solution into the central retinal artery, skin depigmentation and necrosis, bleeding and fat atrophy.
   b. ***Systemic steroids*** administered daily over several weeks may also be effective and are particularly useful if there is a large orbital component.
   c. ***Local resection*** with cutting cautery may reduce the bulk of an anterior circumscribed tumour, but is usually reserved for the late inactive stage.
   d. ***Low-dose radiotherapy.***

Cavernous haemangioma

The cavernous haemangioma is the most common benign orbital tumour in adults, with a female preponderance of 70%. Although it may develop anywhere in the orbit, it most frequently occurs within the muscle cone just behind the globe.

Fig. 17.55
Right axial proptosis due to a cavernous haemangioma

1. **Presentation** is in the fourth to fifth decades with slowly progressive unilateral proptosis. Growth may be accelerated in pregnancy.
2. **Signs**
   - Axial proptosis (Fig. 17.55) which may be associated with optic disc oedema (Fig. 17.56a) and choroidal folds (Fig. 17.56b and c).
   - A lesion at the orbital apex may compress the optic nerve without causing significant proptosis.
   - Gaze-evoked transient blurring of vision may occur.
3. **CT** shows a well-circumscribed oval lesion with slow contrast enhancement.
4. **Treatment** by surgical excision is required in most cases because the lesion gradually enlarges. The cavernous haemangioma, unlike its capillary counterpart, is usually well encapsulated (Fig. 17.56d) and relatively easy to remove.

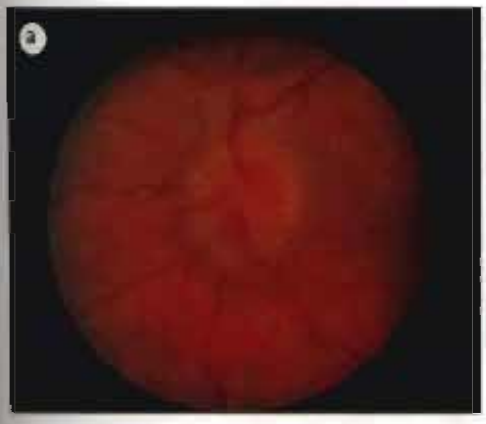
Pleomorphic lacrimal gland adenoma

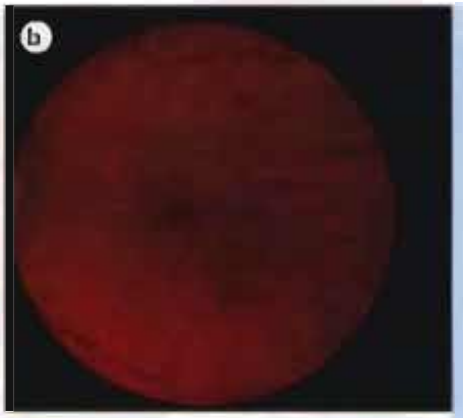
The pleomorphic adenoma (benign mixed-cell tumour) is the most common epithelial tumour of the lacrimal gland and is derived from the ducts, stroma and myoepithelial elements.

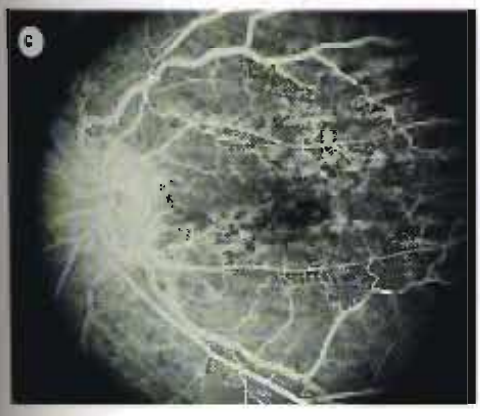
Clinical features

1. **Presentation** is in the fifth decade with a painless, slowly progressive swelling in the superolateral part of the orbit, usually of more than a year's duration.
2. **Signs**
   - A tumour arising from the *orbital lobe* is characterized by a smooth, firm, non-tender mass in the lacrimal gland fossa with inferonasal dystopia (Fig. 17.57).
   - Posterior extension may cause proptosis (Fig. 17.58), ophthalmoplegia and choroidal folds.

Fig. 17.57
Inferonasal dystopia due to pleomorphic adenoma of the orbital lobe of the lacrimal gland (Courtesy of G. Rose)







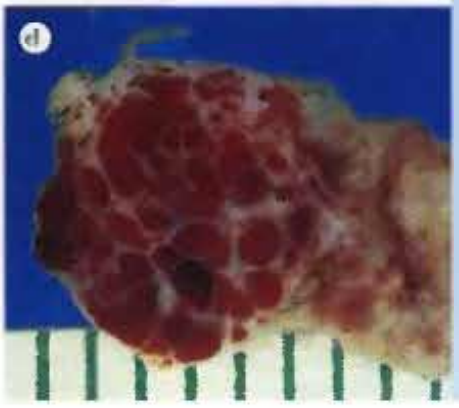


Fig. 17.56
Cavernous haemangioma of the orbit (see text) (Courtesy of Wilmer Institute)

Fig. 17.58
Proptosis due to pleomorphic adenoma of the orbital lobe of the lacrimal gland

Fig. 17.59
Pleomorphic adenoma of the palpebral lobe of the lacrimal gland

- The less common tumour arising from the *palpebral lobe* tends to grow anteriorly, with upper lid swelling, and does not displace the globe (Fig. 17.59).

3. **CT** shows a round or oval mass, with a smooth outline with indentation but not destruction of the bone of the lacrimal gland fossa (Fig. 17.60). The lesion may also indent the globe.

Treatment

This involves surgical excision. If the diagnosis is strongly suspected, it is wise to avoid prior biopsy, to avoid tumour seeding into adjacent orbital tissue, although this may not always be possible in the context of diagnostic uncertainty. Tumours of the palpebral lobe are usually resected, along with a margin of normal tissue, through an anterior (transseptal) orbitotomy. Those of the orbital portion are excised through a lateral orbitotomy as follows:

Fig. 17.60
Axial CT scan showing a right pleomorphic lacrimal gland adenoma with indentation of adjacent bone

a. The temporalis muscle is incised (Fig. 17.61a).
b. The underlying bone is drilled for subsequent wiring (Fig. 17.61b).
c. The lateral orbital wall is removed and the tumour excised (Fig. 17.61c).
d. The temporalis and periosteum are repaired (Fig. 17.61d).

The prognosis is excellent provided excision is complete and without disruption. Incomplete excision or preliminary incisional biopsy may result in seeding of the tumour into adjacent tissues, with recurrences which may later turn malignant.

Lacrimal gland carcinoma

Lacrimal gland carcinoma is a rare tumour which carries a high morbidity and mortality. In order of frequency the main histological types are: (a) *adenoid–cystic*, (b) *pleomorphic adenocarcinoma*, (c) *mucoepidermoid* and (d) *squamous cell*.

Clinical features

1. **Presentation** is in the fourth to sixth decades with a history shorter than that of a benign tumour. Pain, a feature of malignancy, may, however, also occur with inflammatory lesions. A pleomorphic adenocarcinoma (malignant mixed-cell tumour) may present in three main clinical settings:
   - After incomplete or piecemeal excision of a benign pleomorphic adenoma, followed by one or more recurrences over a period of several years with eventual malignant transformation.
   - As a long-standing proptosis (and/or a swollen upper lid) which suddenly starts to increase.

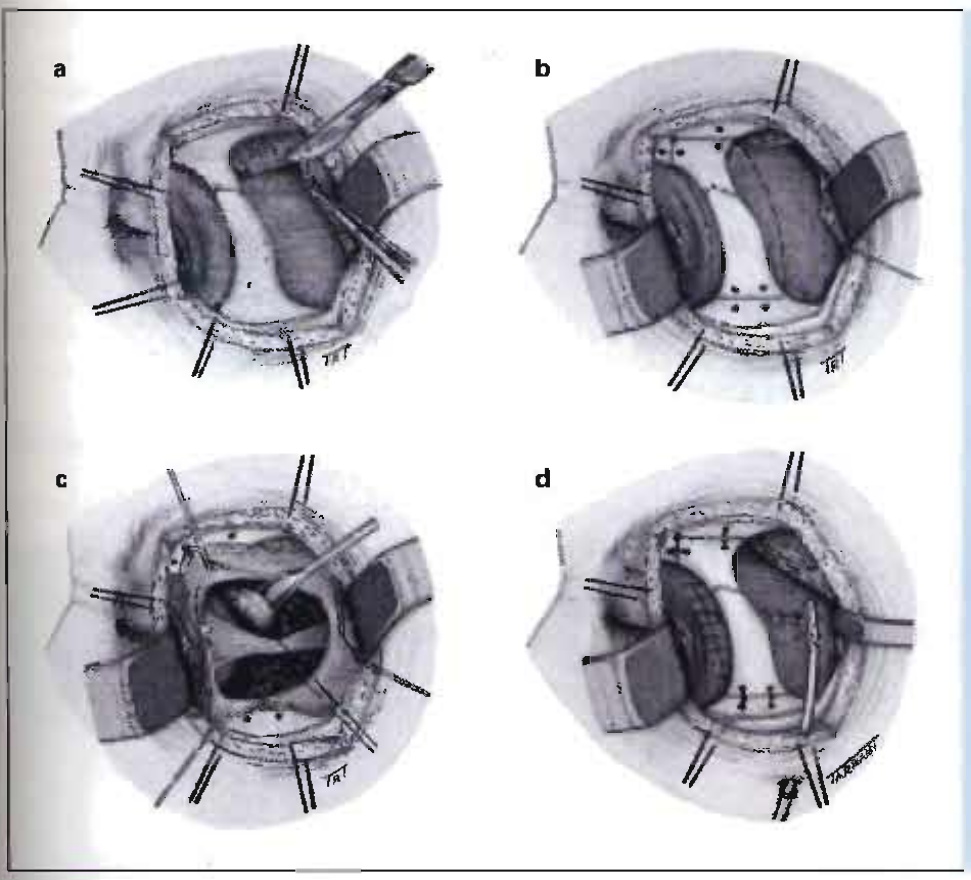


Fig. 17.61
Lateral orbitotomy (see *text*)

- Without a previous history of a pleomorphic adenoma as a rapidly growing lacrimal gland mass (usually of several months' duration).

2. Signs

- A mass in the lacrimal area with inferonasal dystopia (Fig. 17.62).
- Posterior extension, with involvement of the superior orbital fissure, may give rise to conjunctival and episcleral congestion and ophthalmoplegia (Fig. 17.63).
- Limitation of elevation and abduction is common.
- Hypoaesthesia in the region supplied by the lacrimal nerve.
- Optic disc swelling and choroidal folds.

Fig. 17.62
Inferonasal dystopia and ptosis due to lacrimal gland carcinoma (Courtesy of G. Rose)

Fig. 17.63
Periorbital oedema and congestion of the globe due to involvement of the superior orbital fissure by lacrimal gland carcinoma (Courtesy of G. Rose)

3. Investigations

a. ***CT*** shows contiguous erosion or invasion of bone. Calcification in the tumour is commonly seen.

b. ***Biopsy*** is necessary to establish the histological diagnosis. Subsequent management depends on the extent of tumour invasion of adjacent structures as seen on imaging studies.

c. ***Neurological assessment*** is mandatory because adenoid–cystic carcinoma, which spreads perineurally, may extend into the cavernous sinus.

Treatment

1. **Radical surgery**, in the form of orbital exenteration or mid-facial resection, may be attempted. Unfortunately the tumour is almost invariably past total surgical excision, with an extremely poor prognosis for life.
2. **Radiotherapy** combined with local resection may prolong life and reduce pain.

Optic nerve glioma

Optic nerve glioma is a slow-growing pilocytic astrocytoma, which typically affects young girls and occasionally adults. Neurofibromatosis-1 is a common association (*see* Chapter 20).

Clinical features

1. **Presentation** is often towards the end of the first decade with slowly progressive visual loss, followed later by proptosis (Fig. 17.64), although this sequence may occasionally be reversed.
2. **Signs**
   - Optic nerve dysfunction with visual impairment out of proportion to the degree of proptosis.
   - The optic nerve head, initially swollen (Fig. 17.65a), later becomes atrophic.
   - Opticociliary shunt vessels are occasionally seen (*see* Fig. 17.68).
   - Intracranial spread to the chiasm and hypothalamus may develop.
3. **Investigations**
   a. CT shows fusiform enlargement of the optic nerve (Fig. 17.65b).
   b. MRI may show intracranial extension (Fig. 17.66).

Management

This depends on whether the tumour manifests posterior extension.

Fig. 17.64
Severe proptosis due to optic nerve glioma (Courtesy of G. Rose)

Fig. 17.66
Sagittal T1-weighted MRI scan showing invasion of the hypothalamus by an optic nerve glioma in NF-1 (Courtesy of D. Armstrong)

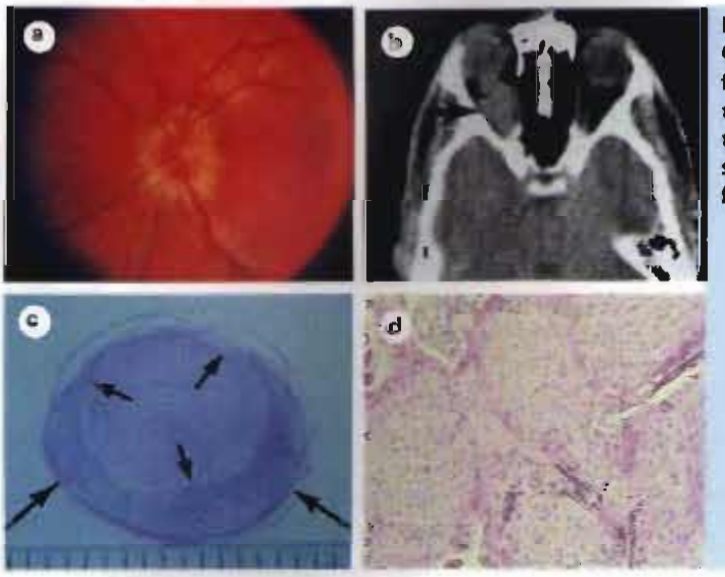


Fig. 17.65
Optic nerve glioma. (a) Disc oedema; (b) axial CT scan showing fusiform enlargement of the optic nerve; (c) short arrows outline the perimeter of the enlarged optic nerve and long arrows show thickening of the arachnoid sheath; (d) high-power section showing increased cellularity and generalized thickening of nerve fibre bundles (Courtesy of Wilmer Institute)

1. **Observation** in patients with no evidence of growth, good vision and no cosmetic deformity.
2. **Surgical excision** with preservation of the globe in patients with growing tumours, particularly if vision is poor and proptosis significant.
3. **Radiotherapy** may be combined with chemotherapy for tumours with intracranial extension that preclude surgical excision.

The prognosis for life is variable. Some tumours have an indolent course with little growth, while others may extend intracranially and threaten life.

Fig. 17.68
Opticociliary shunts (Courtesy of C. Barry)

Optic nerve sheath meningioma

Meningiomas arise from meningothelial cells of the arachnoid villi. Primary orbital meningiomas arising from the optic nerve sheath are, however, rare, representing about 2% of all meningiomas. They are less common than optic nerve gliomas and are more frequently encountered in females.

Clinical features

1. **Presentation** is in middle age with unilateral gradual visual impairment. Transient obscurations of vision may be the presenting symptom.
2. **Signs.** The classical triad is (a) *visual loss*, (b) *optic atrophy* and (c) *opticociliary shunt vessels*. However, the simultaneous occurrence of all three signs in one individual is uncommon. The sequence of involvement is as follows:
   - Optic nerve dysfunction (Fig. 17.67b) and chronic disc swelling (Fig. 17.67a) followed by atrophy.
   - Opticociliary shunt vessels (Fig. 17.68), found in about 30% of cases, regress as optic atrophy supervenes.
   - Restrictive motility defects, particularly in upgaze, because the tumour may 'splint' the optic nerve (*see* Fig. 17.67c).
   - Proptosis caused by intraconal spread usually develops after the onset of visual loss.

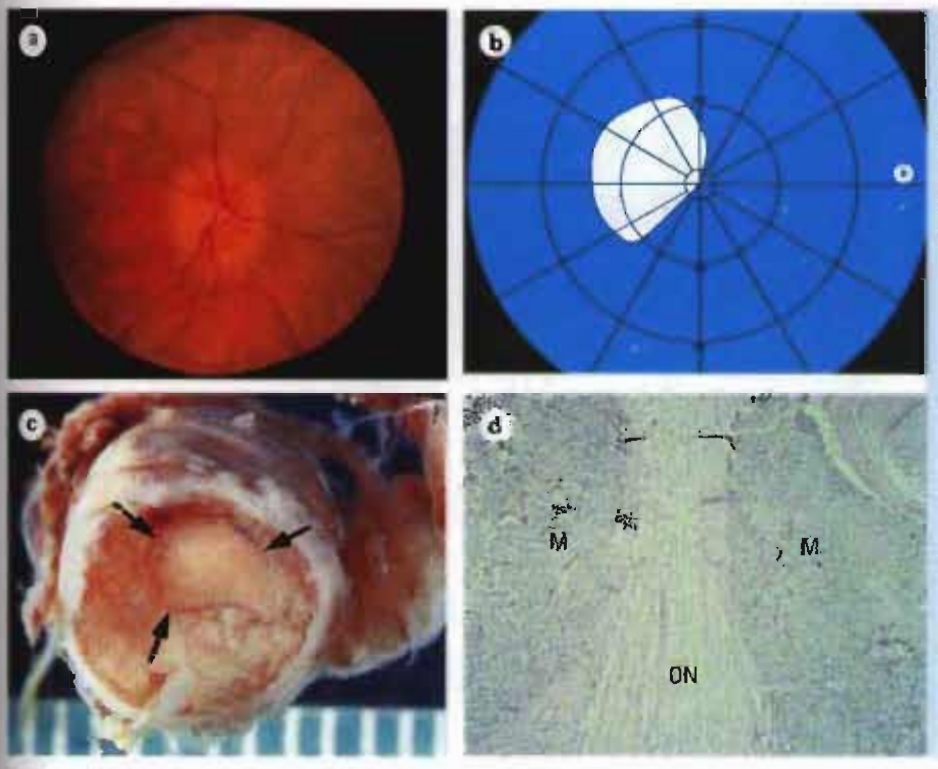


Fig. 17.67
Optic nerve sheath meningioma.
(a) Disc oedema; (b) visual field defect; (c) arrows outline the optic nerve surrounded by meningioma;
(d) high-power section showing the optic nerve (ON) and meningioma (M) (Courtesy of Wilmer Institute)

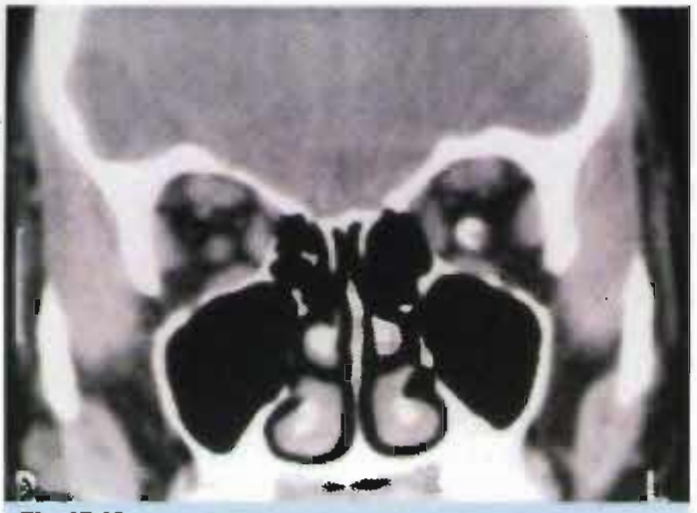


Fig. 17.69
Coronal CT scan showing thickening of the left optic nerve by an optic nerve sheath meningioma

NB: This sequence is the opposite to that seen with tumours outside the dural sheath, in which proptosis develops long before optic nerve compression.

3. **CT** shows tubular thickening and calcification of the optic nerve (Fig. 17.69).

Management

1. **Observation** in middle-aged patients with slow-growing tumours because the prognosis is good.
2. **Surgical excision** in young patients with aggressive tumours, particularly if the eye is also blind.
3. **Radiotherapy** in selected cases.

Fig. 17.70
Periocular involvement by plexiform neurofibroma

The prognosis for life is good in adults, although the tumour may be more aggressive and sometimes fatal in children.

Neurofibroma

Plexiform neurofibroma

Plexiform (diffuse) neurofibroma is the most common peripheral neural tumour of the orbit and occurs almost exclusively in association with neurofibromatosis-1 (*see* Chapter 20).

1. **Presentation** is in early childhood with periorbital swelling.
2. **Signs**
   - Diffuse involvement of the orbit with disfiguring hypertrophy of periocular tissues (Fig. 17.70).
   - Involvement of the eyelids causes mechanical ptosis with a characteristic S-shaped deformity. On palpation the involved tissues feel like a bag of worms.

Fig. 17.71
CT scan showing absence of the greater wing of the left sphenoid bone. **(a)** Coronal view; **(b)** axial view (Courtesy of K. Nischal)

- Pulsation of the globe without a bruit (best detected on applanation tonometry) may be present if there is an associated congenital defect of the greater wing of the sphenoid bone (Fig. 17.71).

3. **Treatment** is extremely difficult. Surgery should be avoided if at all possible because of the intricate relationship between the tumour and important orbital structures.

Isolated neurofibroma

Isolated (localized) neurofibroma is less common and is associated with neurofibromatosis-1 in about 10% of cases.

1. **Presentation** is in the third to fourth decades with insidious mildly painful proptosis unassociated with visual impairment or ocular motility dysfunction.
2. **Treatment** by excision is usually straightforward because the tumour is well circumscribed and relatively avascular.

Lymphomas

Lymphomas of the ocular adnexa (i.e. conjunctiva, lacrimal gland and orbit) constitute approximately 8% of all extranodal lymphomas. They represent one end of the spectrum of lymphoproliferative lesions, at the other end of which lies benign reactive lymphoid hyperplasia. To further compound diagnostic difficulty, a 'grey zone' lies between the two poles of the spectrum in which accurate diagnosis cannot be established by conventional histological techniques.

Classification

The REAL (Revised European–American Lymphoma) classification subdivides lymphomas into five types, with progressive increase in the risk of extranodal disease at diagnosis, of dissemination with time, and of tumour-related death.

- Extranodal marginal-zone B-cell lymphoma.
- Follicle centre lymphoma.
- Diffuse large B-cell lymphoma.
- Plasmacytoma.
- Lymphoplasmocytic lymphoma.

Clinical features

1. **Presentation** is insidious and usually in the sixth to eighth decades.
2. **Signs**
   - Any part of the orbit may be affected, and occasionally involvement is bilateral (Fig. 17.72).
   - Anterior lesions may be palpated and have a rubbery consistency (Fig. 17.73).
   - Occasionally the lymphoma may be confined to the conjunctiva or lacrimal glands, sparing the orbit.
3. **Systemic investigations** in patients with hypercellular lymphoid lesions of the orbit include chest radiographs, serum immunoprotein electrophoresis, thoraco-abdominal CT to detect possible retroperitoneal involvement and, if necessary, bone marrow aspiration.
4. **Course**. This is variable and may be unpredictable. In some patients histological features raise suspicion of malignancy and yet the lesion resolves spontaneously or with the help of steroids. Conversely, what appears to be a benign lymphoid hyperplasia may be followed several years later by the development of lymphoma. Treatment involves radiotherapy for localized lesions and chemotherapy for disseminated disease.

Fig. 17.72
Bilateral orbital lymphoma

Fig. 17.73
Anterior orbital lymphoma

Rhabdomyosarcoma

Rhabdomyosarcoma is the most common childhood primary orbital malignancy. The main role of the ophthalmologist is confined to diagnosis by incisional biopsy followed by prompt referral to a paediatric oncologist.

Clinical features

1. **Presentation** is in the first decade (average 7 years) with rapidly progressive proptosis which may initially mimic an inflammatory process.

2. **Signs**
   - The tumour is most frequently retrobulbar, followed by superior and inferior (Fig. 17.74).
   - A palpable mass and ptosis are present in about one-third of cases (Fig. 17.75).
   - Swelling and injection of overlying skin develop later but the skin is not warm (Fig. 17.76).
   - Parameningeal tumours show bony destruction, lymph node dissemination and involvement of the CNS.
3. **CT** shows a poorly defined mass of homogeneous density often with adjacent bony destruction (Fig. 17.77). In advanced cases tumour spread into the paranasal sinuses may be seen.
4. **Systemic investigations** for evidence of metastatic spread include chest X-ray, liver function tests, bone marrow biopsy, lumbar puncture and skeletal survey. The most common sites for metastases are lung and bone.

Fig. 17.74
Rhabdomyosarcoma (Courtesy of D. Taylor)

Fig. 17.75
Rhabdomyosarcoma (Courtesy of D. Taylor)

Fig. 17.76
Erythema and vascular engorgement of the eyelid associated with rhabdomyosarcoma (Courtesy of M. Szreter)

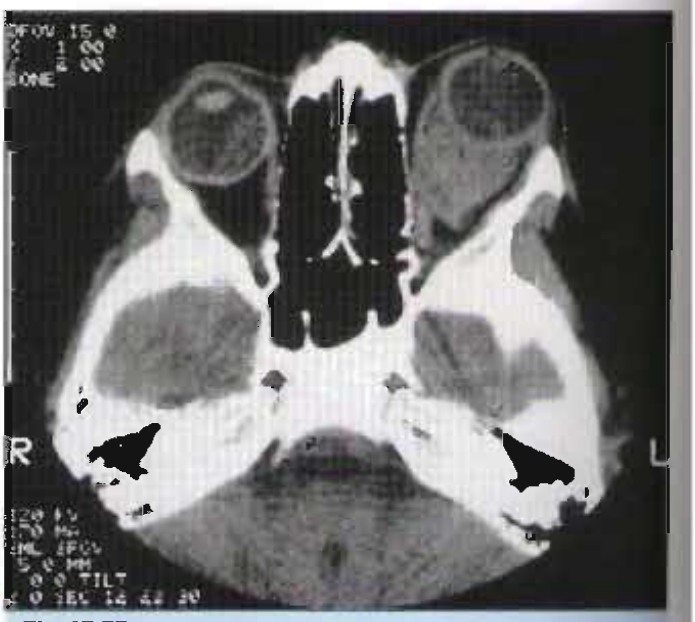


Fig. 17.77
Axial CT scan of a left rhabdomyosarcoma (Courtesy of K. Nischal)

Treatment

1. **Radiotherapy** followed by **chemotherapy** with vincristine, actinomycin and cyclophosphamide.
2. **Surgical excision** is reserved for the rare recurrent or radio-resistant tumour.

The prognosis is dependent on the stage and location of disease at the time of diagnosis. Patients with tumours localized to the orbit have a 95% cure rate.

Differential diagnosis

1. **Orbital cellulitis** typically presents in children with similar acute signs although in rhabdomyosarcoma the skin is not warm.
2. **Granulocytic sarcoma** may also present similarly with a rapidly growing orbital mass (*see* below).

Childhood metastatic tumours

Neuroblastoma

This is one of the most common childhood malignancies. It arises from primitive neuroblasts of the sympathetic chain, most commonly in the abdomen, followed by the thorax and pelvis. Presentation is usually in early childhood; in almost half the cases the tumour is disseminated at diagnosis with

Fig. 17.78
Metastatic neuroblastoma (Courtesy of K. Nischal)

an appalling prognosis. Orbital metastases may be bilateral and typically present with an abrupt onset of proptosis accompanied by a superior orbital mass and lid ecchymosis (Fig. 17.78).

Granulocytic sarcoma (chloroma)

This is a localized tumour composed of malignant cells of myeloid origin. Because the tumour can exhibit a characteristic green colour it was formerly referred to as chloroma. Granulocytic sarcoma may occur as a manifestation of established myeloid leukaemia or it may precede the disease. Presentation is most frequently at about age 7 years with rapid onset of proptosis, sometimes bilateral, which may be associated with ecchymosis and lid oedema (Fig. 17.79). When orbital involvement precedes systemic leukaemia the diagnosis may be difficult.

Langerhans cell histiocytosis (granulomatosis)

This is a rare, poorly understood, multi-system disease characterized by destructive inflammatory lesions that primarily involve bone. Soft tissues are less commonly involved, but cutaneous and visceral involvement may occur. Patients with solitary lesions (eosinophilic granuloma) have a benign course and respond well to treatment. Orbital involvement consists of unilateral or bilateral osteolytic lesions and soft tissue involvement, typically in the superotemporal quadrant (Fig. 17.80).

Fig. 17.79
Advanced granulocytic sarcoma (Courtesy of P. Morse)

Fig. 17.80
Left inferior dystopia due to Langerhans-cell histiocytosis (Courtesy of D. Taylor)

Adult metastatic tumours

Orbital metastases are an infrequent cause of adult proptosis and are much less common than metastases to the choroid. If the orbit is the initial manifestation of the tumour, the ophthalmologist may be the first person to see the patient. In order of frequency the most common primary sites are breast, bronchus, prostate, skin melanoma, gastrointestinal tract and kidney.

1. Presentation

- A mass in the anterior orbit causing dystopia or proptosis is the most common (Fig. 17.81).
- Infiltration of orbital tissues characterized by ptosis, diplopia, brawny indurated periorbital skin and a firm orbit, characterized by resistance to manual retropulsion of the globe.
- Enophthalmos with schirrous tumours.
- Chronic orbital inflammation.
- Primarily with involvement of the cranial nerves (II, III, IV, V, VI) at the orbital apex and only mild proptosis.

2. Special investigations

a. Fine-needle biopsy under CT control is useful for histological confirmation. If this fails, open biopsy may be required.

Fig. 17.81
Right non-axial proptosis due to metastatic hypernephroma

b. Hormonal studies on tissue specimens may be used to guide specific hormone therapy in responsive tumours.

3. **Treatment** is aimed at preserving vision and relieving pain because most patients die within 1 year. Radiotherapy is the mainstay of treatment. Orbital exenteration rarely may be required if other modalities fail to control intolerable symptoms.

Orbital invasion by sinus tumours

Malignant tumours of the paranasal sinuses, although rare, may invade the orbit and carry a poor prognosis unless diagnosed early. It is therefore important to be aware of both their otolaryngological and ophthalmic features.

1. **Maxillary carcinoma** is by far the most common sinus tumour to invade the orbit.
   a. Otolaryngological manifestations include facial pain, congestion and swelling (Fig. 17.82), epistaxis and nasal discharge.
   b. Ophthalmic features include upward dystopia (Fig. 17.83), diplopia and epiphora.
2. **Ethmoidal carcinoma** may cause lateral dystopia.
3. **Nasopharyngeal carcinoma** may spread to the orbit through the inferior orbital fissure. Proptosis is a late finding.

Fig. 17.82
Swelling of the face in advanced carcinoma of the maxillary antrum

Fig. 17.83
Left upward dystopia in carcinoma of the maxillary antrum
(Courtesy of G. Rose)

Craniosynostoses

Craniosynostoses are a group of rare hereditary disorders characterized by premature fusion of cranial sutures accompanied by severe orbital abnormalities. The two most common entities are: (a) *Crouzon syndrome* and (b) *Apert syndrome*.

Crouzon syndrome

Crouzon syndrome is caused primarily by premature fusion of the coronal and saggital sutures. Inheritance is AD, but 25% of cases represent a fresh mutation.

1. **Ocular features**
   - Proptosis due to shallow orbits is the most conspicuous feature (Fig. 17.84). The shallowing is secondary to arrested growth of the maxilla and zygoma. In extreme cases the globes may become luxated anterior to the eyelids.
   - Hypertelorism (wide separation of the orbits).
   - V pattern exotropia and hypertropia.
   - Vision-threatening complications include exposure keratopathy and optic atrophy, due to compression at the optic foramen.
2. **Ocular associations** include aniridia, blue sclera, cataract, ectopia lentis, glaucoma, coloboma, megalocornea and optic nerve hypoplasia.
3. **Systemic features**
   - Short anteroposterior head distance and wide cranium due to premature fusion.
   - Midfacial hypoplasia and curved 'parrot-beak' nose which gives rise to a 'frog-like' facies.
   - Mandibular prognathism.
   - Inverted V-shaped palate.
   - Acanthosis nigricans.

Apert syndrome

Apert syndrome (acrocephalosyndactyly) is the most severe of the craniosynostoses and may involve all the cranial sutures. Inheritence is autosomal dominant, but the majority of cases are sporadic and are associated with older parental age.

Fig. 17.84
Crouzon syndrome

Fig. 17.85
Apert syndrome

1. **Ocular features**
   - Shallow orbits, proptosis and hypertelorism are generally less pronounced than in Crouzon syndrome (Fig. 17.85).
   - Exotropia.
   - Antimongoloid slant of the palpebral apertures.
   - Vision-threatening complications include corneal exposure and optic atrophy.
2. **Ocular associations** include keratoconus, ectopia lentis and congenital glaucoma.
3. **Systemic features**
   - Oxycephaly with flattened occiput and steep forehead.
   - Horizontal groove above the supraorbital ridge.
   - Midfacial hypoplasia with a 'parrot-beak' nose and low-set ears.
   - High-arched palate, cleft palate and bifid uvula.
   - Syndactyly of the hands and feet.
   - Anomalies of the heart, lungs and kidneys.
   - Acneiform skin eruptions on the trunk and extremities.
   - Mental handicap in 30% of cases.

CHAPTER 18

Neuro-ophthalmology

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Neuroimaging

Magnetic resonance imaging

Basic physics

Magnetic resonance imaging (MRI) depends on the rearrangement of hydrogen nuclei (protons—positively charged) when a tissue is exposed to a short electromagnetic pulse. When the pulse subsides, the nuclei return to their normal position, re-radiating some of the energy they have absorbed. Sensitive receivers pick up this electromagnetic echo. Unlike CT it does not subject the patient to ionizing radiation. Exposed tissues produce radiation with characteristic intensity and time patterns. The signals are analysed, computed and displayed as a cross-sectional image which may be: (a) *axial* (Fig. 18.1) (b) *coronal* (Fig. 18.2) or (c) *sagittal* (Figs 18.3, 18.4).

Relaxation times

T1 and T2 weighting refers to two methods of measuring the relaxation times of the excited protons after the magnetic field has been switched off. Various body tissues have different relaxation times so that a given tissue may be T1- or T2-weighted, (i.e. best visualized on that particular type of image). in practice both types of scans are usually performed.

1. **T1-weighted** images are best for normal anatomy (Fig. 18.5 and *see* Fig. 18.3).
   - Hypointense (dark) structures include water and vitreous.
   - Hyperintense (bright) structures include fat and contrast agents.
2. **T2-weighted** images are usually preferred for viewing pathological changes (*see* Figs 18.1 and 18.2).
   - Hypointense structures include fat and contrast agents.
   - Hyperintense structures include vitreous and water.

NB: Bone and calcification are invisible on MRI.

Enhancement

1. **Gadolinium** is a substance which acquires a magnetic moment when placed in an electromagnetic field.

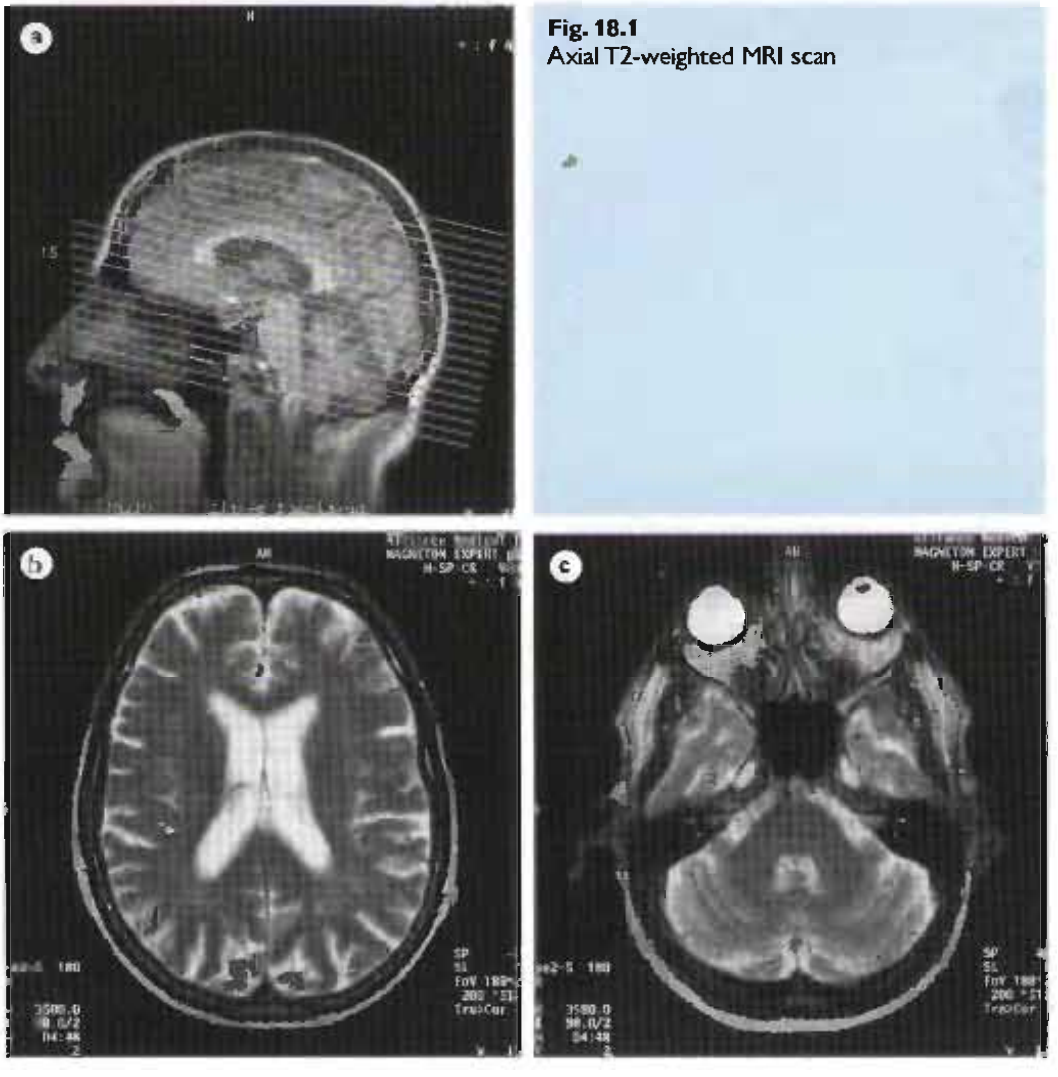


Fig. 18.1
Axial T2-weighted MRI scan

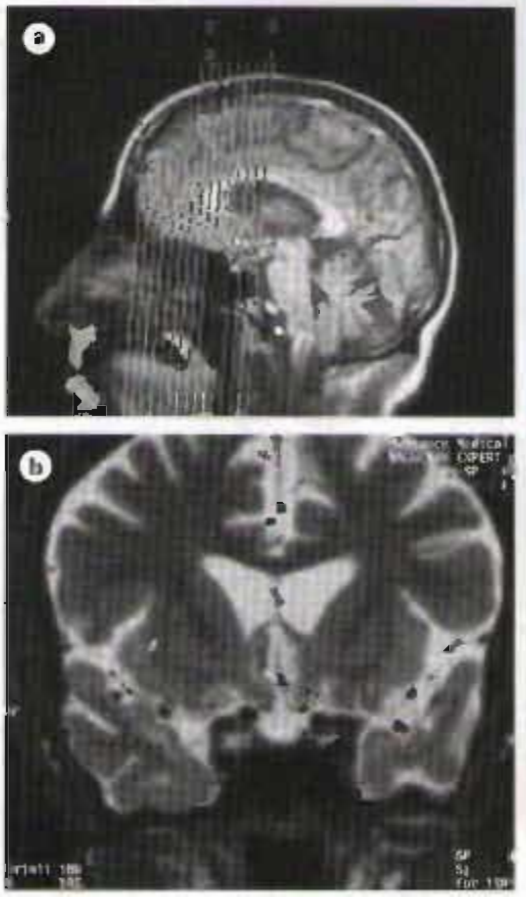


Fig. 18.2
Coronal T2-weighted MRI scan

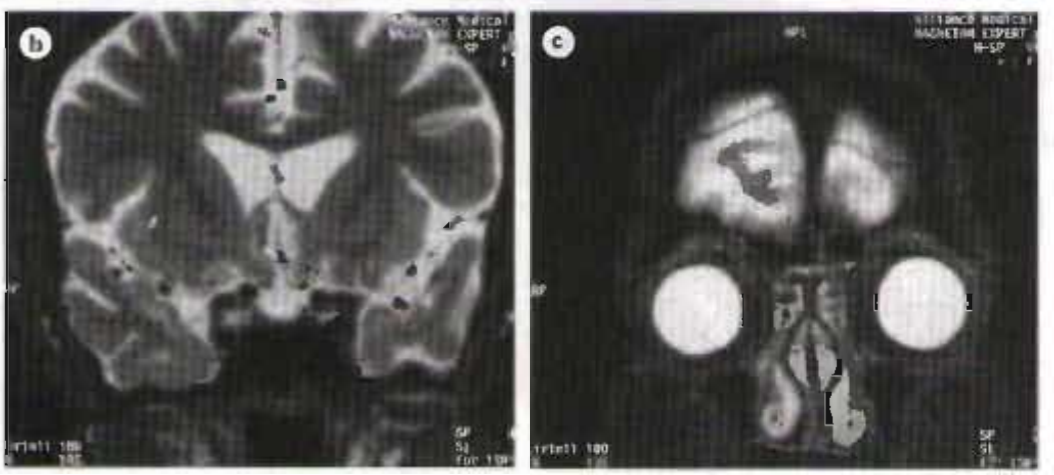


Fig. 18.3
Sagittal T1-weighted MRI scan

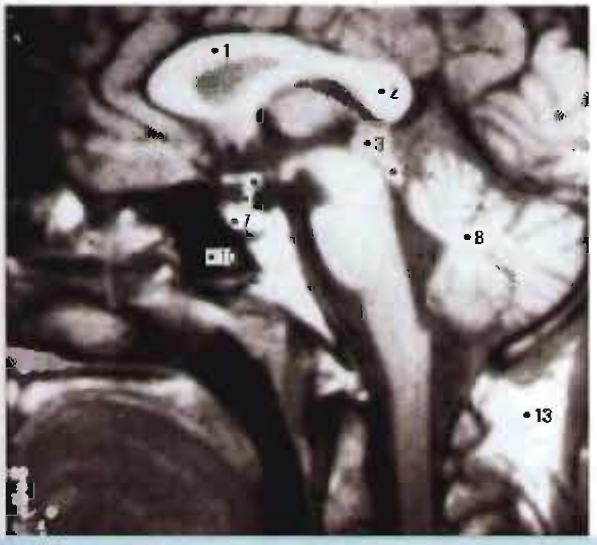


Fig. 18.4
Sagittal MRI scan showing normal anatomy. **(1)** Body of corpus callosum; **(2)** splenium of corpus callosum; **(3)** superior colliculus; **(4)** inferior colliculus; **(5)** infundibular recess; **(6)** infundibulum; **(7)** pituitary gland; **(8)** cerebellum; **(9)** fourth ventricle; **(10)** sphenoid sinus; **(11)** clivus; **(12)** foramen magnum and craniocervical junction; **(13)** subcutaneous fat
(Courtesy of K. Nischal)

Administered intravenously, it remains intravascular unless there is a breakdown of the blood–brain barrier. It is therefore extremely helpful in the detection of tumours and inflammatory lesions which appear bright on T1-weighted scans. Ideally MRI is performed both before (Fig. 18.6) and after (Fig. 18.7) administration of gadolinium. Special head or surface coils can also be used to improve spatial definition of the image. Gadolinium is safer than iodine; adverse effects are uncommon and usually relatively innocuous (e.g. nausea, hives and headache).

2. **Fat suppression** techniques are applied for imaging the orbit because the bright signal of orbital fat on conventional T1-weighted imaging frequently obscures other orbital contents. Fat suppression eliminates this bright signal and better delineates both normal structures (optic nerve and extraocular muscles) as well as tumours, inflammatory lesions and vascular malformations. The combination of gadolinium and fat suppression helps highlight areas of abnormal enhancement that might otherwise remain undetected. However, fat suppression may be associated with various artefacts and therefore should be used in conjunction with, rather than instead of, conventional imaging.

Fig. 18.5
Axial T1-weighted MRI scan

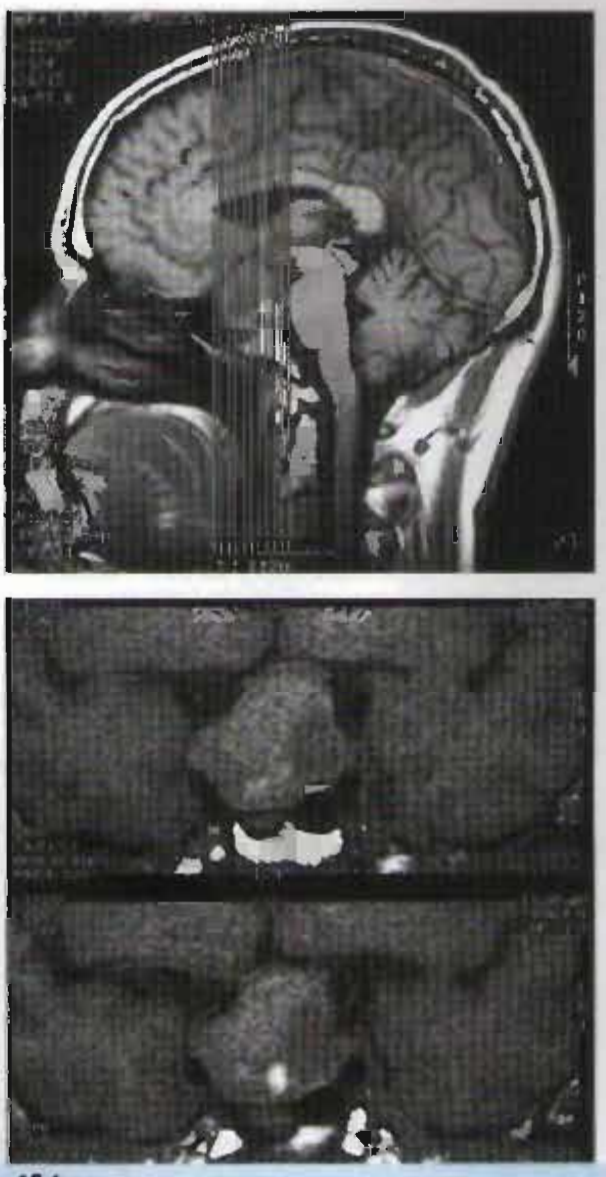


Fig. 18.6
Coronal T1-weighted unenhanced MRI scan of a pituitary adenoma (Courtesy of D. Thomas)

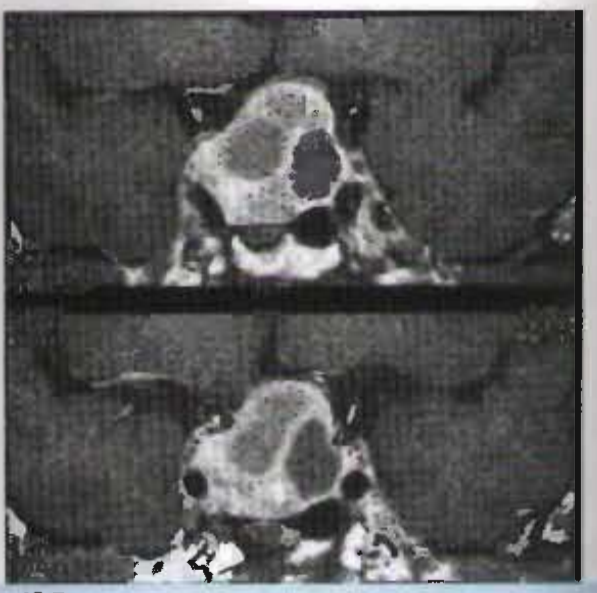


Fig. 18.7
Coronal T1-weighted gadolinium-enhanced MRI scan of a pituitary adenoma (Courtesy of D. Thomas)

Limitations of MRI

- It does not image bone (which appears black), although this is not necessarily a disadvantage.
- It does not detect recent haemorrhage and is therefore inappropriate in patients with acute intracranial bleeding.
- It cannot be used in patients with magnetic foreign objects (e.g. cardiac pacemakers, intraocular foreign bodies).
- It requires the patient to cooperate and remain motionless.
- It is difficult to perform on claustrophobic patients.

Specific neuro-ophthalmic indications

MRI is the technique of choice for lesions of the intracranial pathways. It is important to submit an accurate clinical history to the radiologist and direct attention to specific areas of potential pathology, in order to ensure appropriate imaging.

1. **The optic nerve** is best visualized by contrast-enhanced fat suppression studies using axial and coronal cuts which should include both optic nerve and the brain. MRI can detect lesions of the intraorbital part of the optic nerve (e.g. gliomas) as well as intracranial extension of orbital tumours (Fig. 18.8). In patients with retrobulbar neuritis MRI may display multiple plaques in the periventricular white matter and corpus callosum (*see* Figs 18.24 and 18.25). Since it does not image calcium MRI is not useful in detecting fractures or bony erosion.
2. **Pituitary tumours** are best visualized by contrast-enhanced studies (*see* Fig. 18.7). Coronal slices optimally demonstrate the contents of the sella turcica, while axial cuts demonstrate adjacent structures such as the carotid arteries and cavernous sinuses.
3. **Intracranial aneurysms** can often be visualized by MRI (Fig. 18.9) although intra-arterial angiography may also be required.

Magnetic resonance angiography

Magnetic resonance angiography (MRA) is a non-invasive method of imaging the intra- and extracranial carotids

Fig. 18.8
Axial T1-weighted MRI scan showing a left optic nerve glioma involving the chiasm (Courtesy of D. Armstrong)

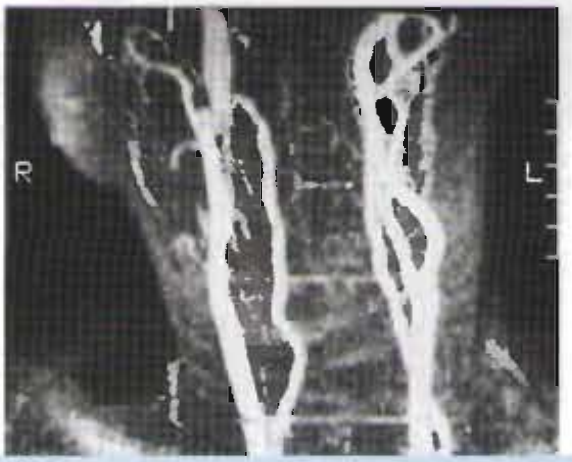


Fig. 18.10
MRA of the extracranial carotid circulation (Courtesy of D. Thomas)

Fig. 18.9
Axial MRI scan showing a right middle cerebral artery aneurysm (Courtesy of D. Thomas)

Fig. 18.11
Coronal CT scan showing a right orbital blow-out fracture

(Fig. 18.10) and vertebrobasilar circulations to demonstrate abnormalities such as stenosis, occlusion, arteriovenous malformations and aneurysms. However, MRA is not as reliable as conventional intra-arterial angiography in detecting aneurysms smaller than 5 mm in diameter. Conventional angiography therefore remains the 'gold standard' for accurate diagnosis and planning of surgery for berry aneurysms (*see* Fig. 18.11b) which have caused third nerve palsies or subarachnoid haemorrhage. Even if MRA demonstrates an aneurysm, conventional angiography is ideally still required to identify additional undetected aneurysms.

Computed tomography

Computed tomography (CT) uses thin X-ray beams to obtain tissue density values from which detailed cross-sectional images are formed by a computer. The cuts may be coronal or axial but not sagittal. Lesions with intrinsic vasculature may be better visualized by iodinated contrast agents.

Clinical indications

In general, CT is easier and faster to perform than MRI but exposes the patient to ionizing radiation.

- The main advantage over MRI lies in detecting bony lesions such as fractures and erosions, and demonstrating skull anatomy. CT is therefore very useful for evaluating patients with orbital trauma and can display fractures (Fig. 18.11) and foreign bodies as well as blood, herniation of extraocular muscles and emphysema.
- CT can also detect intraocular calcification (optic disc drusen and retinoblastoma).
- CT is preferable for acute cerebral (Fig. 18.12) or subarachnoid haemorrhage because the lesions may not appear on MRI for hours.
- CT is as good or superior to MRI with fat suppression in demonstrating enlarged extraocular muscles in thyroid eye disease (*see* Fig. 17.16).
- CT can be used when MRI is contraindicated (i.e. patients with ferrous foreign bodies).

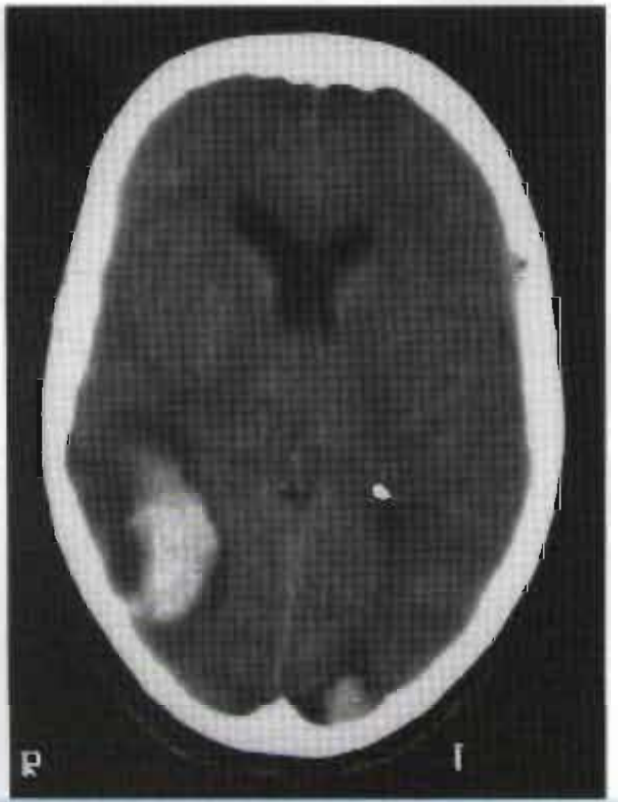


Fig. 18.12
Axial CT scan showing acute intracerebral haemorrhages
(Courtesy of L. Webb)

Optic nerve

Applied anatomy

General structure

1. **Afferent fibres.** The optic nerve carries about 1.2 million afferent nerve fibres, which originate in the retinal ganglion cells. Most of these synapse in the lateral geniculate body, although some reach other centres, notably the pre-tectal nuclei in the midbrain. Nearly one-third of the fibres subserve the central 5° of the visual field. Within the optic nerve itself the nerve fibres are divided into about 600 bundles (each containing 2000 fibres) by fibrous septa derived from the pia mater (Fig. 18.13).
2. **Oligodendrocytes** provide axonal myelination. Congenital myelination of retinal nerve fibres is the result of anomalous intraocular extension of these cells.
3. **Microglia** are immunocompetent phagocytic cells which probably modulate apoptosis (programmed death) of retinal ganglion cells.
4. **Astrocytes** line the spaces between axons and other structures. When axons are lost in optic atrophy astrocytes fill in the empty spaces.
5. **Surrounding sheaths**
   a. ***Pia mater*** is the delicate innermost sheath containing blood vessels.
   b. ***Subarachnoid space*** is continuous with the cerebral subarachnoid space and contains cerebrospinal fluid (CSF).
   c. ***Outer sheath*** comprises the arachnoid mater and the tougher dura mater. The latter is continuous with the sclera. Optic nerve fenestration involves incision of the outer sheath.

Anatomical subdivisions

The optic nerve is approximately 50 mm long from globe to chiasm and can be subdivided into four segments:

1. **Intraocular** segment (optic disc, nerve head) is the shortest, being 1 mm deep and 1.5 mm in vertical diameter. Neurological disorders affecting this part of the optic nerve include inflammation (papillitis), oedema and abnormal deposits (drusen). In relation to the lamina cribrosa the intraocular segment can be further subdivided into three zones:
   - The prelaminar zone is supplied by very small branches of the central retinal artery.
   - The laminar and postlaminar zones are supplied by branches of the short posterior ciliary arteries via the anastomotic circle of Zinn (which also receives input

from the parapapillary choroid and pial arterial network).

2. **Intraorbital** segment is 25–30 mm long and extends from the globe to the optic foramen at the orbital apex. Its diameter is 3–4 mm because of the addition of the myelin sheaths to the nerve fibres. At the orbital apex the nerve is surrounded by the tough fibrous annulus of Zinn, from which originate the four rectus muscles. Because the superior and medial rectus muscles partly originate from the nerve sheath itself, inflammatory optic neuropathy (e.g. retrobulbar neuritis) may be associated with pain on ocular movement. Within the orbit the optic nerve is slack and S-shaped, allowing for eye movements without stretching.

NB: Because of this redundancy the optic nerve does not become unduly stretched until proptosis is severe.

3. **Intracanalicular** segment traverses the optic canal and measures about 6 mm. Unlike the intraorbital portion it is fixed to the canal, since the dura mater fuses with the periosteum.
4. **Intracranial** segment joins the chiasm and varies in length from 5 to 16 mm (average 10 mm). Long intracranial segments are particularly vulnerable to damage by adjacent lesions such as pituitary adenomas and aneurysms.

Axoplasmic transport

Axoplasmic transport is the movement of cytoplasmic organelles within a neurone between the cell body and the terminal synapse (Fig. 18.14a and b). Orthograde transport involves movement from cell body to synapse and retrograde transport is characterized by the converse. Rapid axoplasmic transport is an active mechanism requiring oxygen and is energized by ATP. Axoplasmic flow may be interrupted by a variety of insults including hypoxia and toxins which interfere with ATP production. Retinal cotton wool spots are the result of accumulation of organelles due to interruption of axoplasmic flow between the retinal ganglion cells and their terminal synapses. Papilloedema is similarly caused by hold-up of axoplasmic flow at the lamina cribrosa (Fig. 18.14c and d).

Evaluation of optic nerve disease

Signs of optic nerve dysfunction

1. **Reduced visual acuity** for distance and near is common (but may also occur with a great variety of other disorders).
2. **Afferent pupillary defect** (*see* later).

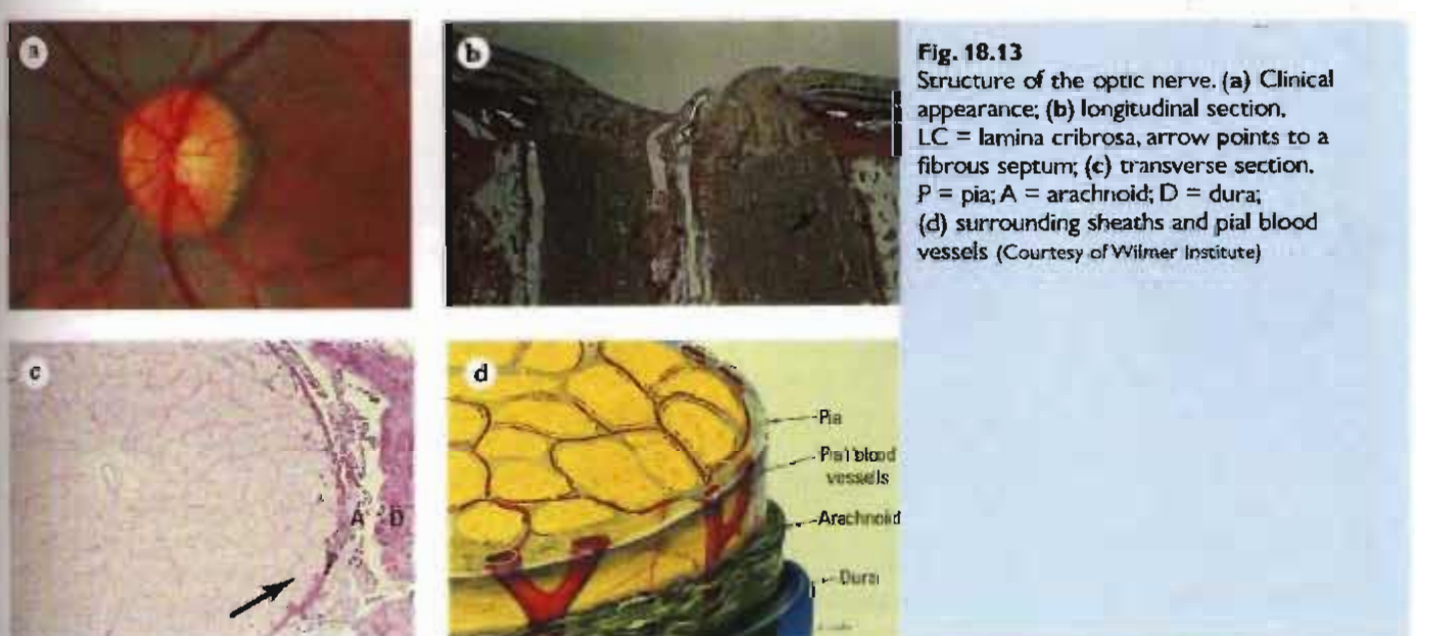


Fig. 18.13
Structure of the optic nerve. **(a)** Clinical appearance; **(b)** longitudinal section. LC = lamina cribrosa, arrow points to a fibrous septum; **(c)** transverse section. P = pia; A = arachnoid; D = dura; **(d)** surrounding sheaths and pial blood vessels (Courtesy of Wilmer Institute)

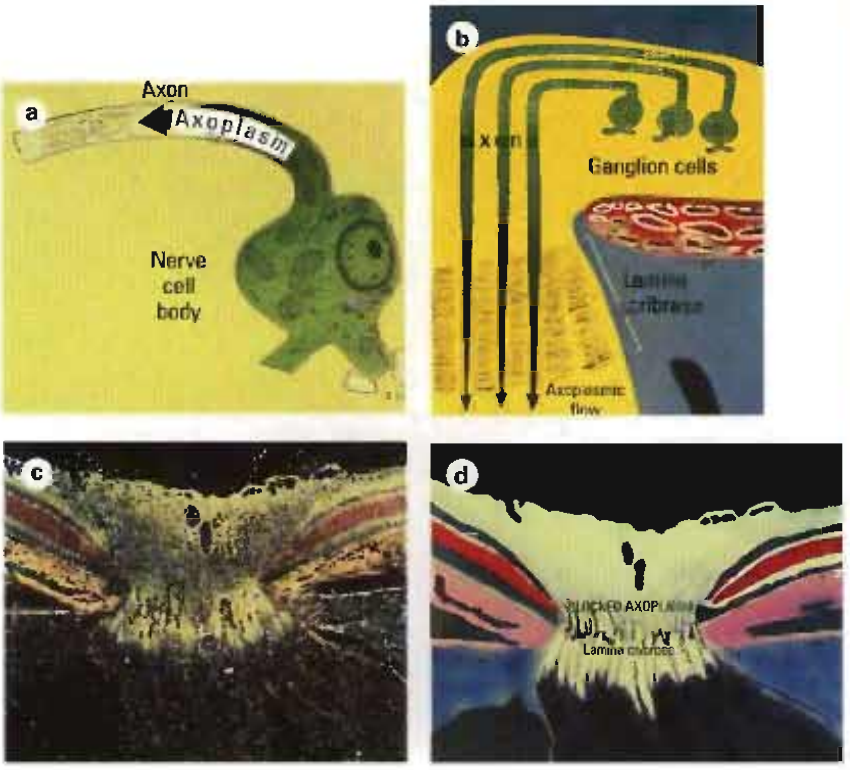


Fig. 18.14
(a and b) Axoplasmic flow; (c and d) interrupted axoplasmic flow at the lamina cribrosa in papilloedema (Courtesy of Wilmer Institute)

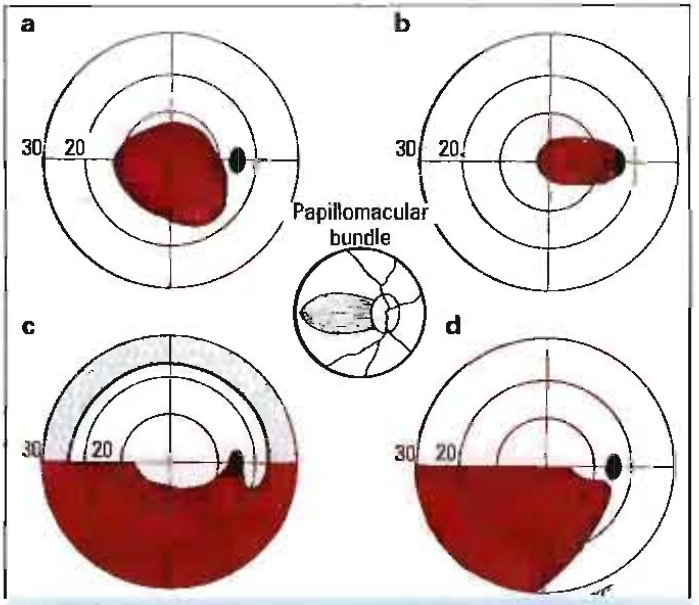


Fig. 18.15
Visual field defects in optic nerve disease. (a) Central scotoma; (b) centrocaecal scotoma; (c) nerve fibre bundle; (d) altitudinal

3. **Dyschromatopsia** (impairment of colour vision), which mainly affects red and green. A simple way of detecting a unilocular colour vision defect is to ask the patient to compare the colour of a red object between the two eyes. More accurate assessment requires the use of Ishihara pseudo-isochromatic plates, a City University chart or the Farnsworth–Munsell 100-hue test (*see* Chapter 13).
4. **Diminished light brightness sensitivity**, which may persist after visual acuity returns to normal (as seen after a previous attack of optic neuritis). This is best demonstrated as follows:
   a. A light from an indirect ophthalmoscope is shone first into the normal eye and then into the eye with the suspected optic nerve lesion.
   b. The patient is asked whether the light is symmetrically bright in both eyes.
   c. The patient will report that the light appears less bright in the affected eye.
   d. The patient is requested to assign a relative value to the brightness of the light in the diseased eye, as compared with the normal eye.
5. **Diminished contrast sensitivity**, which is tested by asking the patient to identify gratings of gradually increasing contrast, over a range of spatial frequencies (the Arden plates). This is very sensitive to subtle visual loss, although it is not specific to optic nerve disease. Contrast sensitivity may also be estimated with the Pelli–Robson chart, in which letters of gradually diminishing contrast (arranged in triplets) are read.
6. **Visual field defects**, which vary with the underlying pathology, include diffuse depression of the central visual field, central scotomas, centrocaecal scotomas, nerve fibre bundle and altitudinal (Fig. 18.15).

Optic disc changes

There is no direct correlation between the appearance of the optic disc and visual function. The four main appearances in acquired optic nerve disorders are the following:

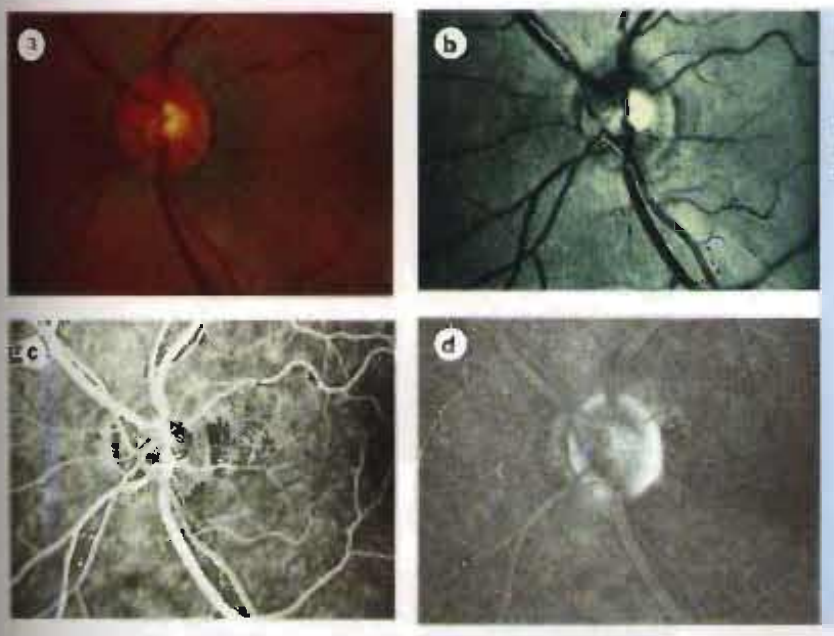


Fig. 18.16
Normal optic disc. (a) Clinical appearance; (b) red-free photography showing retinal nerve fibre striations; (c) venous phase FA, (d) late phase FA showing slight hyperfluorescence of the disc due to staining (Courtesy of Wilmer Institute)

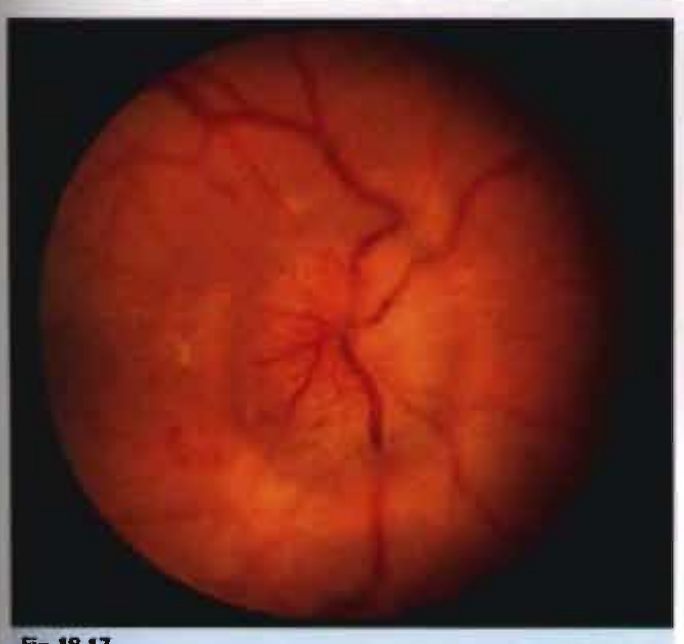


Fig. 18.17
Disc swelling due to papilloedema

Fig. 18.18
Opticociliary shunts

1. **Normal disc** (Fig. 18.16) is classically associated with retrobulbar neuritis, although the disc may initially appear normal in Leber optic neuropathy and compressive lesions.
2. **Disc swelling** (Fig. 18.17) is a feature of papilloedema, anterior ischaemic optic neuropathy, papillitis and the acute stage of Leber optic neuropathy. It may also occur with compressive lesions before the development of optic atrophy.
3. **Opticociliary shunts** (Fig. 18.18) represent retinochoroidal venous collaterals at the optic disc, and develop as a compensatory mechanism for chronic venous compression most frequently caused by optic nerve sheath meningioma and occasionally optic nerve glioma.
4. **Optic atrophy**, which represents the end result of almost any of the aforementioned clinical conditions (*see* later).

Special investigations

1. **Manual kinetic perimetry** (Goldmann) is useful in the evaluation of neuro-ophthalmological disease, since it affords assessment of the peripheral field.
2. **Automated perimetry** quantitates the threshold retinal sensitivity to a static target. The most useful strategy tests the central 30° with points straddling the midline (e.g. Humphrey 30-2).
3. **MRI** is the method of choice for imaging the optic nerves. The orbital segment of the optic nerve is best demonstrated by fat suppression techniques by which the bright signal from orbital fat in T1-weighted images is eliminated.

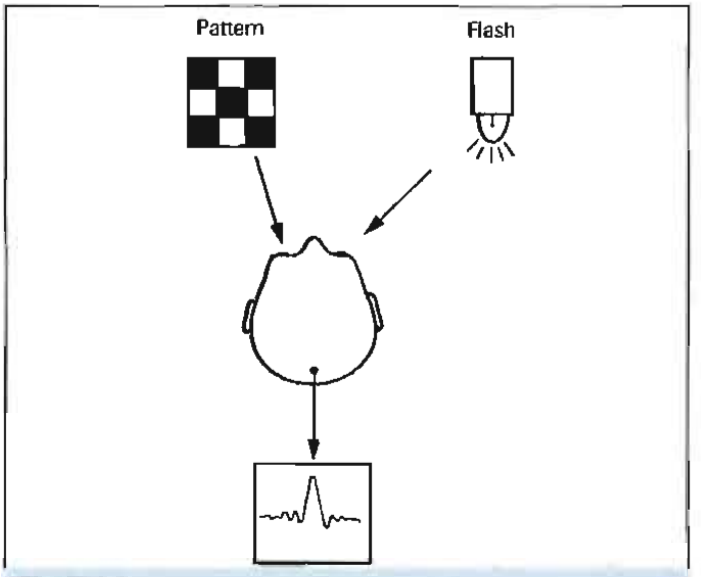


Fig. 18.19
Principles of visually evoked potential

The intracanalicular and intracranial segments are better visualized on MRI than CT because of the absence of bony artefacts with the former.

4. **Visually evoked potential** (VEP) is a recording of electrical activity of the visual cortex created by stimulation of the retina. The stimulus is either a flash of light (flash VEP) or a black-and-white checker-board pattern, which periodically reverses polarity on a screen (pattern VEP) (Fig. 18.19). Several tests are performed and the average potential is calculated by a computer. Both latency (delay) and amplitude of the VEP are assessed. In optic neuropathy both parameters are affected, with prolongation of latency and decrease in amplitude of the VEP.
5. **Fluorescein angiography** (FA) may occasionally be helpful in the differentiation of papilloedema, in which there is disc leakage (*see* Fig. 18.50), from optic disc drusen, which do not leak, but auto-fluoresce (*see* Fig. 18.48).

Optic atrophy

Optic atrophy, an important sign of advanced optic nerve disease, may be primary or secondary.

Primary optic atrophy

This occurs without antecedent swelling of the optic nerve head. It may be caused by lesions affecting the visual pathways from the retrolaminar portion of the optic nerve to the lateral geniculate body. Lesions anterior to the optic chiasm result in unilateral optic atrophy, whereas those involving the chiasm and optic tract will cause bilateral optic atrophy.

1. **Causes**
   - Following retrobulbar neuritis.
   - Compressive lesions such as tumours and aneurysms (this may also result in secondary atrophy).
   - Hereditary optic neuropathies.
   - Toxic and nutritional optic neuropathies.
2. **Signs** (Fig. 18.20)
   - Pale, flat disc with clearly delineated margins.
   - Reduction in number of small blood vessels on the disc surface (Kestenbaum sign).
   - Attenuation of parapapillary blood vessels and thinning of the retinal nerve fibre layer.
   - The atrophy may be diffuse or sectoral depending on the cause and level of the lesion. For example, optic atrophy caused by chiasmal lesions may involve the nasal and temporal portions of the disc, but spare the superior and inferior (bow-tie atrophy) (*see* Fig. 18.106).

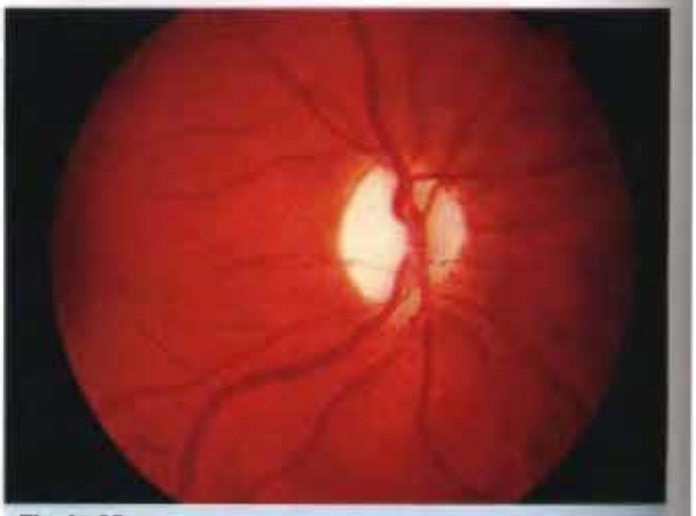


Fig. 18.20
Primary optic atrophy

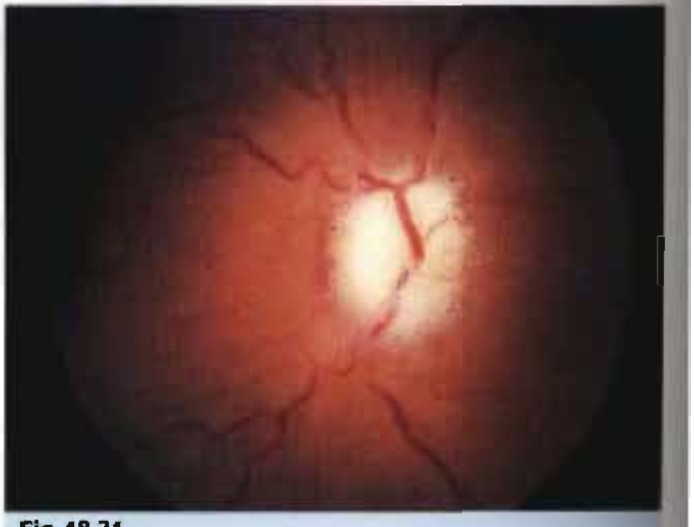


Fig. 18.21
Secondary optic atrophy

NB: Temporal pallor, however, may indicate atrophy of fibres from the papillo-macular bundle, which enter the optic nerve head on the temporal side.

Secondary optic atrophy

Secondary optic atrophy is preceded by swelling of the optic nerve head.

1. **Causes** include chronic papilloedema, anterior ischaemic optic neuropathy and papillitis.
2. **Signs** vary according to the cause. The main features are (Fig. 18.21):
   - White or dirty grey, slightly raised disc with poorly delineated margins due to gliosis.
   - Reduction in number of small blood vessels on the disc surface.

Optic neuritis

Optic neuritis is an inflammatory, infective or demyelinating process affecting the optic nerve. It can be classified both ophthalmoscopically and aetiologically as follows.

Ophthalmoscopic classification

1. **Retrobulbar neuritis**, in which the optic disc appearance is normal, at least initially, because the optic nerve head is not involved. It is the most frequent type in adults and is frequently associated with multiple sclerosis (MS).
2. **Papillitis**, in which the pathological process affects the optic nerve head primarily, or secondary to contiguous retinal inflammation. It is characterized by variable hyperaemia and oedema of the optic disc, which may be associated with parapapillary flame-shaped haemorrhages (Fig. 18.22). Cells in the posterior vitreous may be seen. Papillitis is the most common type of optic neuritis in children, although it can also affect adults.
3. **Neuroretinitis** is characterized by papillitis in association with inflammation of the retinal nerve fibre layer. A macular star figure composed of hard exudates may not be present initially, but becomes apparent within a few days or weeks and tends to become more prominent as the optic disc swelling is resolving (Fig. 18.23). In some cases there is associated parapapillary retinal oedema and serous elevation of the macula. Neuroretinitis is the least common type of optic neuritis and is most frequently associated with viral infections and cat-scratch fever. Other causes include syphilis and Lyme disease. In most cases it is a self-limiting disorder which resolves within 6–12 months.

Fig. 18.22
Papillitis

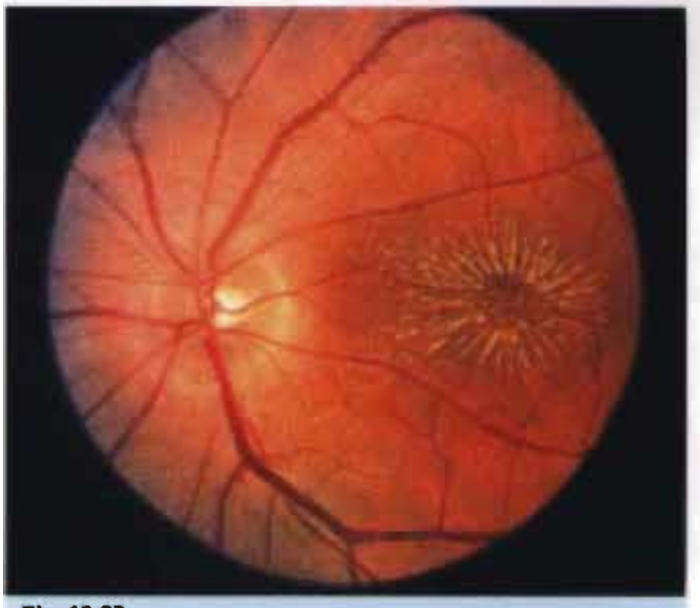


Fig. 18.23
Neuroretinitis

> ***NB:*** Neuroretinitis is never a manifestation of demyelination.

Aetiological classification

1. **Demyelinating**, which is by far the most common cause.
2. **Parainfectious**, which may follow a viral infection or immunization.
3. **Infectious**, which may be sinus-related, or associated with cat-scratch fever, syphilis, Lyme disease, cryptococcal meningitis in patients with AIDS and herpes zoster.
4. **Autoimmune**, which may be associated with systemic autoimmune diseases.

Demyelination

Demyelination is a pathological process by which normally myelinated nerve fibres lose their insulating myelin layer. The myelin is phagocytosed by microglia and macrophages, subsequent to which astrocytes lay down fibrous tissue (the plaque). A demyelinating disease disrupts nervous conduction within the white matter tracts within the brain, brain stem and spinal cord; peripheral nerves are not involved.

1. **Demyelinating diseases** which may cause ocular problems are the following:
   a. ***Isolated optic neuritis***, with no clinical evidence of generalized demyelination, although in a high proportion of cases this subsequently develops.
   b. ***Multiple sclerosis*** (MS), which is by far the most common (*see* Chapter 20).

c. *Devic disease* (neuromyelitis optica), which is a rare disease that may occur at any age. It is characterized by bilateral optic neuritis and subsequent development of transverse myelitis (demyelination of the spinal cord) within days or weeks.

d. *Schilder disease*, which is a very rare, relentlessly progressive, generalized disease with an onset prior to the age of 10 years and death within 1–2 years. Bilateral optic neuritis without subsequent improvement may occur.

2. **Ocular features**

a. *Visual pathway lesions* most frequently involve the optic nerves and cause optic neuritis. Demyelination may occasionally involve the optic chiasm, and rarely the optic tracts or radiations.

b. *Brain stem lesions* may result in internuclear ophthalmoplegia and gaze palsies, ocular motor cranial nerve palsies, trigeminal and facial nerve palsies and nystagmus.

3. **Association of optic neuritis with MS.** Although some patients with optic neuritis have no clinically demonstrable associated systemic disease, the following close association exists between optic neuritis and MS.

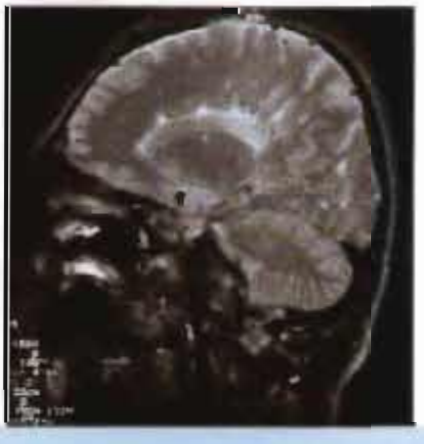


Fig. 18.24
Sagittal T1-weighted MRI scan showing periventricular plaques of demyelination

Fig. 18.25
Axial T2-weighted MRI scan showing periventricular plaques of demyelination

- Patients who develop optic neuritis but have a normal brain MRI have a 16% probability of developing MS within 5 years.
- At the first episode of optic neuritis, approximately 50% of patients with no other signs of MS will show demyelinating lesions on MRI (Figs 18.24 and 18.25). These patients carry a high risk of developing clinical MS within 5–10 years.
- Evidence of optic neuritis may be found in 70% of established MS cases.
- In a patient with optic neuritis the subsequent risk of MS is increased with winter onset, HLA-DR2 positivity and Uhtoff phenomenon (worsening of symptoms on elevation of body temperature, such as with exercise or a hot bath).

Demyelinating optic neuritis

1. **Presentation** is with subacute monocular visual impairment; rarely both eyes are involved simultaneously. Discomfort in or around the eye is common and frequently exacerbated by ocular movements. The discomfort may precede or accompany the visual loss and usually lasts a few days. Frontal headache and tenderness of the globe are present in some patients.
2. **Signs**
   - Visual acuity is usually between 6/18 and 6/60 although rarely it may be reduced to no light perception.
   - The optic disc is normal in the majority of cases (retrobulbar neuritis); the remainder show papillitis.
   - Temporal disc pallor may be seen in the fellow eye indicative of previous optic neuritis.
   - Dyschromatopsia is universal and frequently worse than would be expected for that level of visual impairment.
   - Other features of optic nerve dysfunction are present, as previously described.
3. **Visual field defects**
   - The most common is diffuse depression of sensitivity in the entire central 30°, followed in frequency by altitudinal/arcuate defects and then by focal central/centrocaecal scotomas.
   - Focal defects are frequently accompanied by an element of superimposed generalized depression.
   - The asymptomatic fellow eye may also manifest visual field loss at presentation.
4. **Course.** Recovery typically begins within 2–3 weeks and continues over a period of 6 months, when maximal recovery is reached.
5. **Prognosis.** Approximately 75% of patients recover visual acuity to 6/9 or better; 85% recover to 6/12 or better, even if visual acuity was reduced to no light perception during the attack. However, despite return of visual acuity other parameters of visual function, such as colour vision, contrast sensitivity and light brightness appreciation, often remain abnormal. A mild afferent pupillary defect may persist and optic atrophy may ensue, particularly following recurrent attacks.

6. Treatment

a. Indications

- When the presenting visual loss is mild, treatment is probably unnecessary.
- When visual acuity within the first week of onset is worse than 6/12, treatment may speed up recovery by several weeks. This is relevant in the context of bilateral acute involvement, which is uncommon, or those who have poor vision in the fellow eye.

b. Regimen

- Intravenous methylprednisolone sodium succinate (1 g daily) for 3 days followed by oral prednisolone (1 mg/kg daily) for 11 days.

c. Benefits

- Delays further neurological events consistent with MS by 2 years.
- Hastens visual recovery from optic neuritis but does not appear to have any long-term benefit on final visual acuity.

NB: Oral steroids alone are contraindicated because they offer no benefit and double the recurrence rate of optic neuritis. Intramuscular interferon beta-1a at the time of the first episode of optic neuritis is beneficial in reducing the development of clinical demyelination in patients at high risk of MS based on the presence of subclinical brain MRI lesions.

Parainfectious optic neuritis

Optic neuritis may be associated with various viral infections such as measles, mumps, chickenpox, rubella, whooping cough and glandular fever. It may also occur following immunization. Children are affected much more frequently than adults.

1. **Presentation** is usually 1–3 weeks following a viral infection with acute severe visual loss, which may involve both eyes. This may be associated with other neurological features such as headache, seizures or ataxia (meningoencephalitis).
2. **Signs.** The optic discs most frequently manifest bilateral papillitis although occasionally there may be a neuroretinitis or the discs may be normal.
3. **Treatment** is not required in the vast majority of patients because the prognosis for spontaneous visual recovery is very good. However, when visual loss is severe and bilateral or involves an only seeing eye, intravenous steroids should be considered.

Infectious optic neuritis

1. **Sinus-related** optic neuritis is an infrequent condition characterized by recurrent attacks of unilateral visual loss associated with severe headache and spheno-ethmoidal sinusitis. Possible mechanisms of optic neuropathy include direct spread of infection, occlusive vasculitis and bony defects in the wall of the sinus. Treatment is with systemic antibiotics and, if appropriate, surgical drainage.
2. **Cat-scratch fever** (benign lymphoreticulosis) is a self-limiting systemic infection characterized by regional lymphadenopathy preceded by a cat-scratch (*see* Chapter 20). The organism is susceptible to doxycycline, rifampicin, ciprofloxacin and co-trimoxazole. The prognosis is excellent, with recovery of vision within 1–4 weeks of starting therapy.
3. **Syphilis** may cause acute papillitis or neuroretinitis during the primary or secondary stages (*see* Chapter 20). Involvement may be unilateral or bilateral and is frequently associated with a mild vitritis.
4. **Lyme disease** (borreliosis) is a spirochaetal infection transmitted by a tick bite. It may cause neuroretinitis and occasionally acute retrobulbar neuritis, associated with other neurological manifestations, which may mimic MS (*see* Chapter 20). Treatment of neurological involvement is with intravenous ceftriaxone 2 g daily for 14 days.
5. **Cryptococcal** meningitis in patients with AIDS may be associated with acute optic neuritis, which may be bilateral.
6. **Varicella zoster virus** most frequently causes papillitis by spread from contiguous retinitis (i.e. acute retinal necrosis, progressive outer retinal necrosis). Primary optic neuritis is uncommon but may occur in immunocompromised patients, some of whom may subsequently develop viral retinitis. Treatment is with intravenous antiviral agents.

Non-arteritic anterior ischaemic optic neuropathy

Pathogenesis

Non-arteritic anterior ischaemic optic neuropathy (NAION) is a partial or total infarction of the optic nerve head caused by occlusion of the short posterior ciliary arteries. It typically occurs as an isolated event in patients between the ages of 45 and 65 years with structural crowding of the optic nerve head so that the physiological cup is either very small or absent. Predisposing systemic conditions include hypertension, diabetes mellitus, hypercholesterolaemia, collagen vascular disease, antiphospholipid antibody syndrome, sudden hypotensive events and cataract surgery.

Clinical features

1. **Presentation** is with sudden, painless, monocular visual loss which is not associated with premonitory visual obscurations. Visual loss is frequently discovered on awakening, suggesting that nocturnal hypotension may play an important role.
2. **Signs**
   a. Visual acuity, in about 30% of patients, is normal or only slightly reduced. The remainder have moderate to severe impairment.

*b. **Visual field defects*** are typically inferior altitudinal but central, paracentral, quadrantic and arcuate defects may also be seen.

*c. **Dyschromatopsia*** is proportional to the level of visual impairment in contrast to optic neuritis in which colour vision may be severely impaired when visual acuity is reasonably good.

*d. **Disc*** is pale with diffuse or sectoral oedema which may be surrounded by a few splinter-shaped haemorrhages (Fig. 18.26a). The oedema gradually resolves and pallor ensues (Fig. 18.27a).

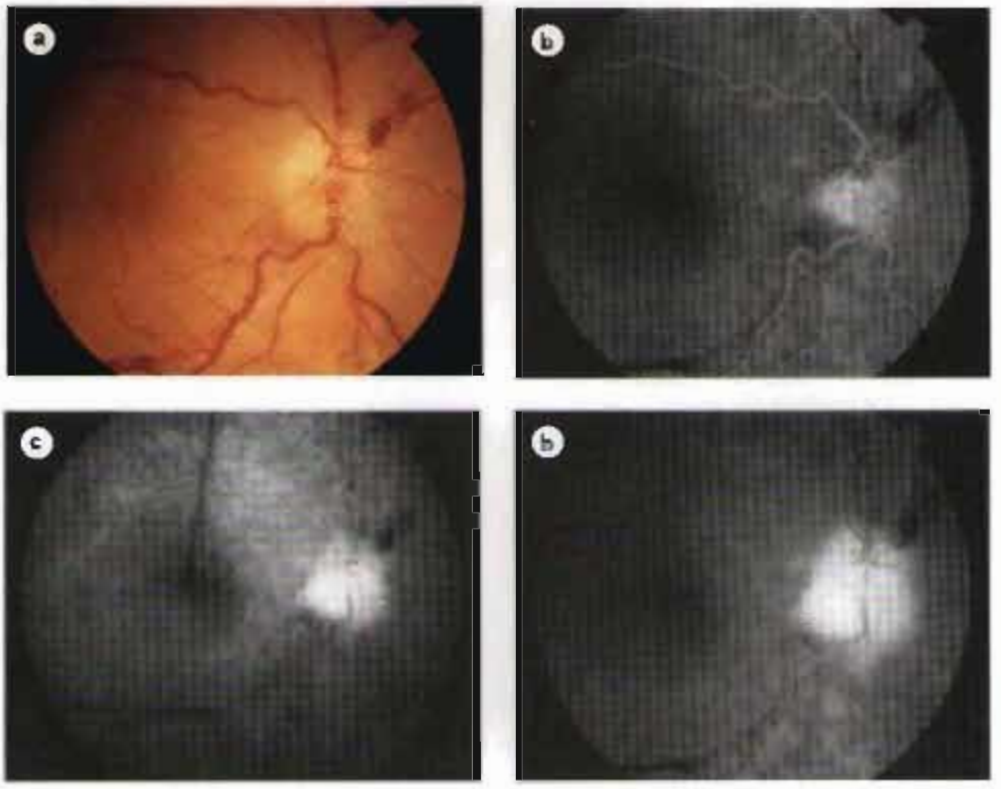


Fig. 18.26
Acute non-arteritic anterior ischaemic optic neuropathy (see text) (Courtesy of S. Milewski)

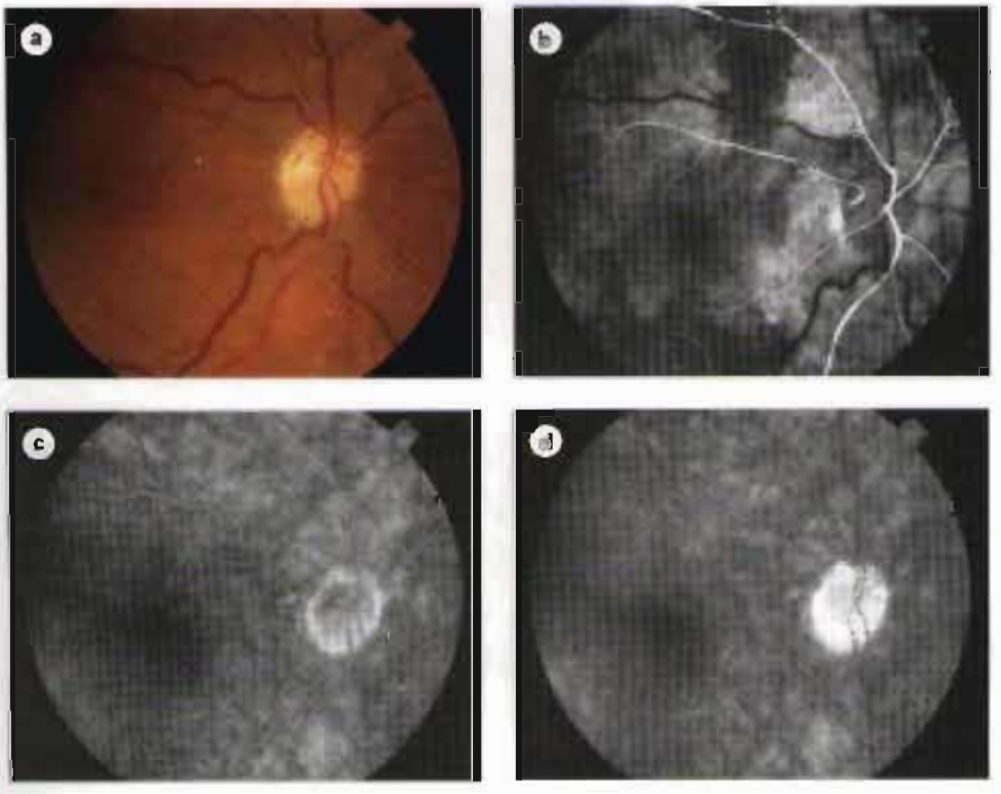


Fig. 18.27
Optic atrophy following non-arteritic anterior ischaemic optic neuropathy (see text) (Courtesy of S. Milewski)

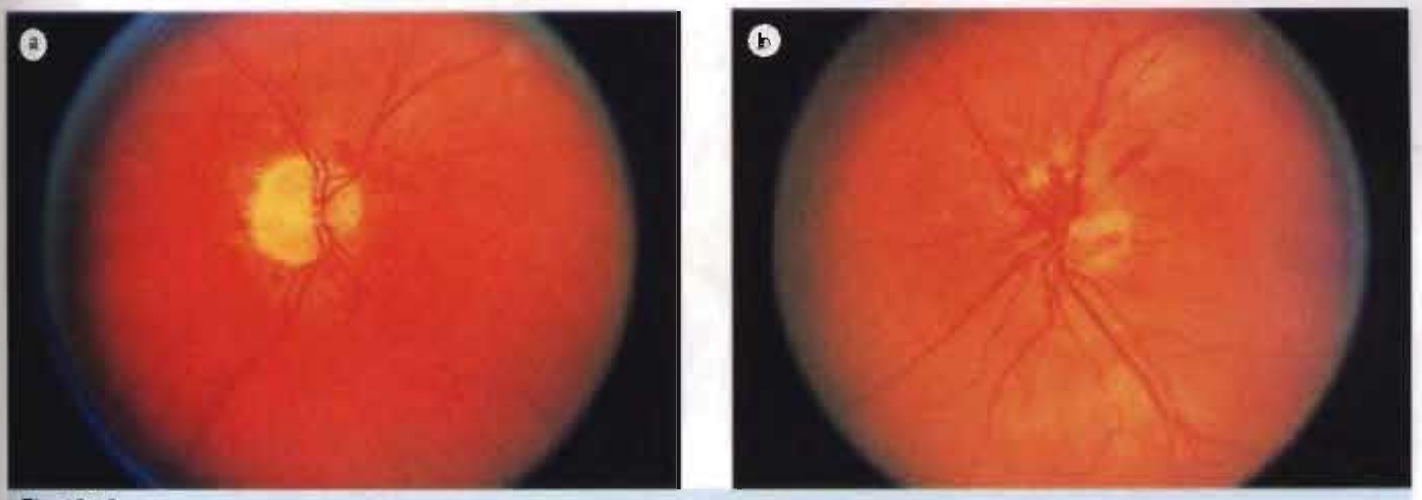


Fig. 18.28
Pseudo-Foster Kennedy syndrome associated with non-arteritic anterior ischaemic optic neuropathy (see text) (Courtesy of Wilmer Institute)

3. **FA** during the acute stage shows localized disc hyperfluorescence (Fig. 18.26b) which becomes more intense and then eventually involves the entire disc (Fig. 18.26c and d). Once optic atrophy develops, FA shows unequal choroidal filling during the arterial phase (Fig. 18.27b); the late stages show increasing disc hyperfluorescence (Fig. 18.27c and d).
4. **Special investigations** include serological studies, fasting lipid profile and blood glucose. It is also very important to exclude occult giant cell arteritis and other autoimmune diseases.

Prognosis

There is no definitive treatment although any underlying systemic predispositions should be treated and smoking discouraged. In most patients there is no further loss of vision although, in a small percentage, visual loss continues for 6 weeks. Between 30% and 50% develop involvement of the fellow eye within months or years although this may be reduced with aspirin. When the second eye becomes involved, optic atrophy in one eye (Fig. 18.28a) and disc oedema in the other (Fig. 18.28b) gives rise to the 'pseudo-Foster Kennedy syndrome'.

NB: AION never recurs in the same eye.

Arteritic anterior ischaemic optic neuropathy

Giant cell arteritis (GCA) (*see* Fig. 18.30b) is a medical emergency because prevention of blindness depends on prompt recognition and treatment. The disease typically affects patients older than 65 years and has a predilection for medium-sized and large arteries, particularly the superficial temporal, ophthalmic, posterior ciliary and the proximal part of the vertebral. The severity and extent of involvement are associated with the quantity of elastic tissue in the media and adventitia of the artery. For this reason, the intracranial arteries, which possess little elastic tissue, are usually spared. The four most important diagnostic criteria of GCA are: (a) jaw claudication, (b) neck pain, (c) C-reactive protein >2.45 mg/dl and ESR >47 mm/hour (*see* Chapter 20). Ocular complications of GCA include the following:

1. **Arteritic anterior ischaemic optic neuropathy** (AAION) is the most common (Fig. 18.29). In untreated patients the incidence is 30–50%, of which one-third develop bilateral involvement.
2. **Transient ischaemic attacks** (amaurosis fugax) may precede infarction of the optic nerve head.

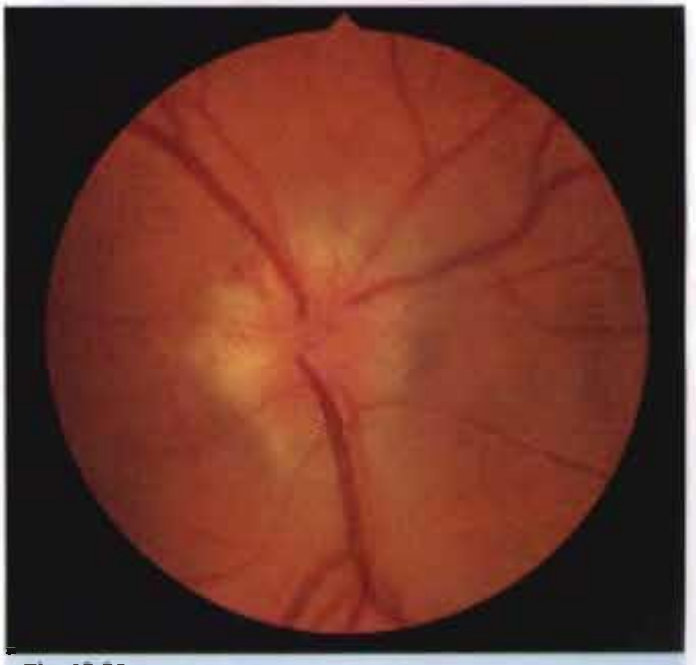


Fig. 18.29
Arteritic anterior ischaemic optic neuropathy

3. **Cotton wool spots** are uncommon. They are probably caused by platelet microembolization from the partially thrombosed ophthalmic or central retinal artery. Because GCA is a disease of medium-sized or large arteries, it does not involve terminal arterioles to produce cotton wool spots.
4. **Cilioretinal artery occlusion** may be combined with AAION (*see* Fig. 14.78).
5. **Central retinal artery occlusion** is usually combined with occlusion of a posterior ciliary artery. This is because the central retinal artery often arises from the ophthalmic artery by a common trunk with one or more of the posterior ciliary arteries. However, ophthalmoscopy shows occlusion of only the central retinal artery; the associated ciliary occlusion can be detected only on FA.
6. **Ocular ischaemic syndrome** due to involvement of the ophthalmic artery is rare (*see* Chapter 15).
7. **Diplopia**, transient or constant, may be caused by ischaemia of the ocular motor nerves or extraocular muscles.

Clinical features

1. **Presentation** is with sudden, profound unilateral visual loss which may be accompanied by periocular pain and preceded by transient visual obscurations and flashing lights. Bilateral simultaneous involvement is rare. Most cases occur within a few weeks of the onset of GCA although at presentation about 20% of patients do not have systemic symptoms (i.e. occult GCA).
2. **Signs** (in chronological order)
   - Pale and swollen optic disc with small splinter-shaped haemorrhages on its margin (Fig. 18.30a).
   - Over 1–2 months, the swelling gradually resolves (Fig. 18.30c) and severe optic atrophy ensues with profound impairment of visual function (Fig. 18.30d).
3. **FA** shows severe hypoperfusion of the choroid.
4. **Prognosis** is very poor because visual loss is usually permanent although, very rarely, prompt administration of systemic steroids may be associated with partial visual recovery.

Treatment

The aim of treatment is to prevent blindness of the fellow eye although, in a few unfortunate patients, the second eye also becomes blind despite prompt steroid administration.

1. **Regimen**
   - Intravenous methylprednisolone 1 g/day for 3 days together with oral prednisolone 80 mg daily.
   - After 3 days the oral dose is reduced to 60 mg and then 50 mg for 1 week each.
   - The daily dose is then reduced by 5 mg weekly; headache, ESR and C-reactive protein permitting, until 10 mg is reached.
   - Maintenance daily therapy is ideally 10 mg, although higher doses may be required to control headache.

> ***NB:*** Temporal artery biopsy should be performed, ideally within 3 days of starting treatment. Histological confirmation of GCA will justify long-term steroid administration.

2. **Duration** of treatment is governed by the patient's symptoms and the level of the ESR or C-reactive protein. Symptoms may, however, recur without a corresponding rise in ESR or C-reactive protein and vice versa. Most patients need treatment for 1–2 years, although some may require indefinite maintenance therapy.

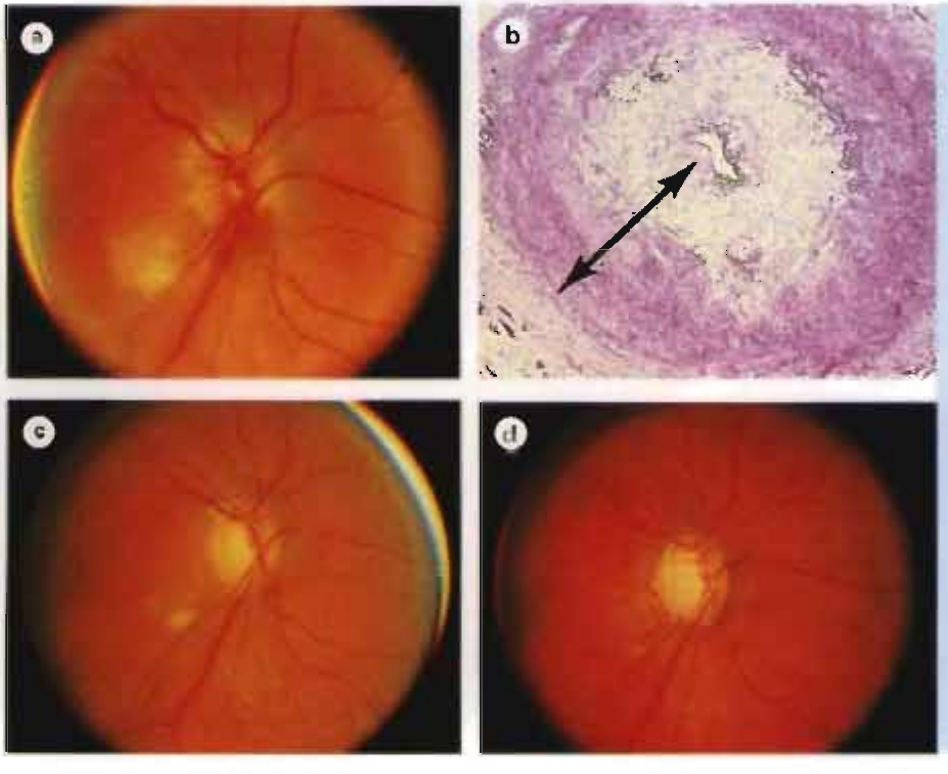


Fig. 18.30
Giant cell arteritis. (a, c and d) Progression of anterior ischaemic optic neuropathy (see text); (b) transverse section of an artery showing granulomatous inflammation involving all layers of the wall and constricting the lumen (arrows) (Courtesy of Wilmer Institute)

NB: Injudicious use of steroids may cause greater harm than the disease itself. Steroid-induced complications may necessitate the use of steroid-sparing agents such as azathioprine.

Diabetic papillopathy

Diabetic papillopathy is an uncommon condition characterized by transient visual dysfunction associated with optic disc swelling which may occur in both type 1 and type 2 diabetics. The underlying pathogenesis is unclear but may be the result of small-vessel disease.

1. **Presentation** is usually with milder optic nerve dysfunction and slower progression than in NAION or optic neuritis.
2. **Signs**
   - Visual acuity is usually 6/12 or better.
   - Unilateral or bilateral, mild disc swelling and hyperaemia (Fig. 18.31).
   - Disc surface telangiectasia is common, and when severe may be mistaken for neovascularization on cursory examination.
   - Visual field defects in the form of generalized constriction or central scotomas.
   - Relative afferent pupillary defects may be seen in unilateral/asymmetric disease.
   - Dyschromatopsia may be present.
3. **Prognosis** is relatively good despite the lack of definitive treatment. Systemic steroids are of questionable benefit and tend to compromise diabetic control. In most cases spontaneous resolution occurs within several months, with stabilization or improvement of visual acuity, although mild optic atrophy may ensue.

Leber hereditary optic neuropathy

Leber hereditary optic neuropathy (LHON) is a rare disease which is the result of maternal mitochondrial DNA mutations (3460, 14484, 11778, and 15257). The majority of patients are males in their twenties with the 11778 mutation. In atypical cases the condition may affect females and present at any age between 10 and 60 years. The diagnosis of LHON should therefore be considered in any patient with bilateral optic neuritis, irrespective of age.

1. **Presentation** is typically with unilateral, acute, severe, painless visual loss. The fellow eye becomes similarly affected within days or weeks (but no longer than 2 months) after the first.
2. **Signs** during the acute stage are often subtle and easily overlooked; in some patients the disc may be entirely normal.
   - In typical cases there are dilated capillaries on the disc surface which may extend onto adjacent retina (telangiectatic microangiopathy), vascular tortuosity and swelling of the parapapillary nerve fibre layer (Fig. 18.32). Telangiectatic microangiopathy may be present in asymptomatic female relatives.
   - Subsequently, the telangiectatic vessels regress and severe optic atrophy ensues.

NB: Surprisingly, the pupillary light reactions may remain fairly brisk.

3. **FA** shows absence of dye leakage.
4. **Visual field defects** usually consist of centrocaecal scotomas.
5. **Prognosis** is poor, although some visual recovery may occur in a minority of cases even years later. Most patients suffer severe, bilateral and permanent visual loss with a final visual acuity of 6/60 or less. The 11778 mutation carries the worst prognosis.

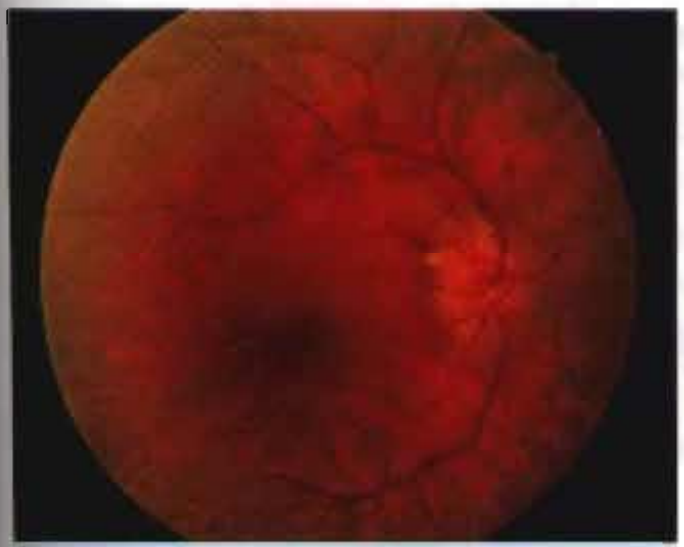


Fig. 18.31
Diabetic papillopathy

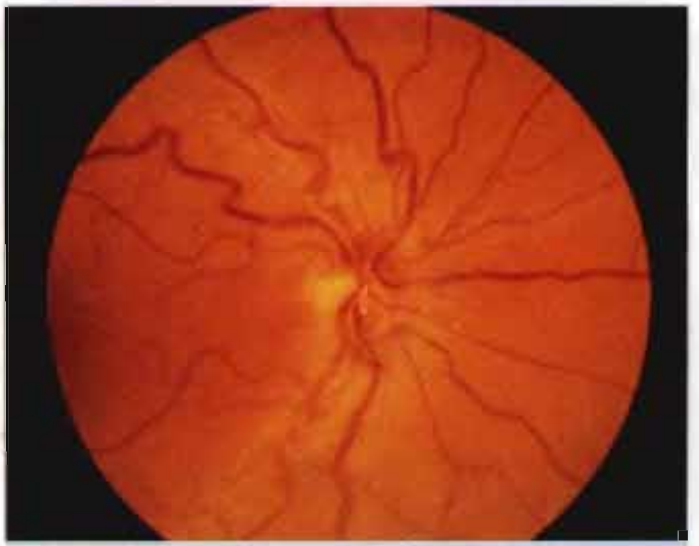


Fig. 18.32
Acute stage of Leber optic neuropathy

6. **Treatment** is generally ineffective although many modalities, including steroids, hydroxocobalamin and surgical intervention, have been tried. Smoking and excessive consumption of alcohol should be discouraged, to minimize potential stress on mitochondrial energy production.

Hereditary optic atrophies

The hereditary optic atrophies (neuropathies) are a very rare heterogeneous group of disorders that are primarily characterized by bilateral optic atrophy.

Kjer syndrome

1. **Inheritance** is AD.
2. **Presentation** is usually in the first decade with insidious visual loss.
3. **Signs**. Mild temporal or diffuse optic atrophy.
4. **Prognosis** is variable (final visual acuity 6/12–6/60) with considerable variation within and between families.
5. **Systemic abnormalities** are absent.

Behr syndrome

1. **Inheritance** is AR.
2. **Presentation** is in the first decade with visual loss which stabilizes after a variable period of progression.
3. **Signs**. Diffuse optic atrophy.
4. **Prognosis** is variable with moderate to severe visual loss and nystagmus.
5. **Systemic abnormalities** include spastic gait, ataxia and mental handicap.

Wolfram syndrome

This is also refered to as DIDMOAD = Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness.

1. **Inheritance** is AR.
2. **Presentation** is between the ages of 5 and 21 years.
3. **Signs**. Diffuse optic atrophy.
4. **Prognosis** is very poor (final visual acuity is <6/60).

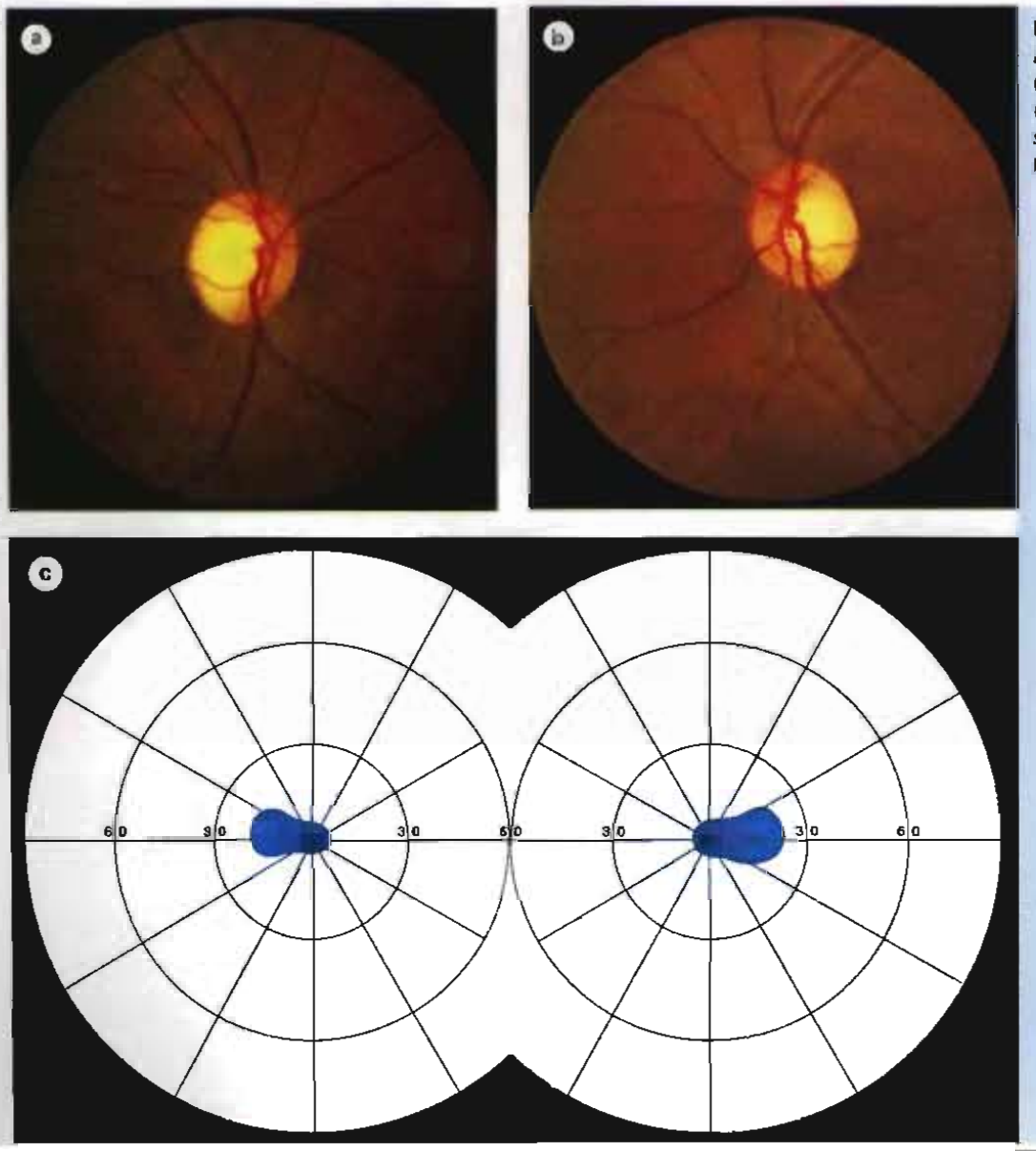


Fig. 18.33 Alcohol–tobacco amblyopia. (a and b) Temporal disc pallor; (c) bilateral centrocaecal scotomas (Courtesy of Wilmer Institute)

5. **Systemic abnormalities** (apart from DIDMOAD), include anosmia, ataxia, seizures, mental handicap, short stature, endocrine abnormalities and elevated CSF protein.

Alcohol–tobacco amblyopia

Alcohol–tobacco amblyopia typically affects heavy drinkers and cigar and pipe smokers who are deficient in protein and the B vitamins. Most patients have neglected their diet, obtaining their calories from alcohol instead.

1. **Presentation** is with insidious onset, progressive, bilateral, usually symmetrical visual impairment associated with dyschromatopsia.
2. **Signs.** The optic dics at presentation are normal in most cases. Some patients show subtle temporal pallor, splinter-shaped haemorrhages on or around the disc, or minimal disc oedema.
3. **Visual field defects** are bilateral, relatively symmetrical, centrocaecal scotomas (Fig. 18.33c). The margins of the defects are difficult to define with a white target but are easier to plot and larger when using a red target.
4. **Treatment** involves weekly injections of 1000 units of hydroxocobalamin for 10 weeks. Multivitamins are also administered and patients should be advised to eat a well-balanced diet and abstain from drinking and smoking.
5. **Prognosis** is good in early cases provided patients comply with treatment although visual recovery may be slow. In advanced and unresponsive cases there is permanent visual loss as a result of optic atrophy (Fig. 18.33a and b).

Drug-induced optic neuropathies

Ethambutol

Ethambutol (Myambutol, Mynah) is used in combination with isoniazid and rifampicin in the treatment of tuberculosis. Toxicity is dose- and duration-dependent, the incidence being 6% at a daily dose of 25 mg/kg; rarely 15 mg/kg may be toxic. Toxicity is unusual and may occur after 2 months of therapy (average is 7 months).

> *NB:* Isoniazid may also rarely cause toxic optic neuropathy, particularly in combination with ethambutol.

1. **Presentation** is with symmetrical insidious visual impairment associated with dyschromatopsia.
2. **Signs** include normal or slightly swollen optic discs with splinter-shaped haemorrhages.
3. **Visual field defects** usually consist of central or centrocaecal scotomas although bitemporal or peripheral constriction may occur.
4. **Prognosis** is good following cessation of treatment although recovery may take up to 12 months. A minority of patients develop permanent visual impairment as a result of optic atrophy.
5. **Screening** should be at about 3-monthly intervals if the daily dose exceeds 15 mg/kg. The drug should be stopped immediately if symptoms develop.

Amiodarone

Amiodarone is used to treat cardiac arrhythmias. Vortex keratopathy, which is innocuous, is virtually universal (*see* Chapter 5). Optic neuropathy, however, occurs in only 1–2% of patients and is not dose-related.

1. **Presentation** is with insidious unilateral or bilateral visual impairment.
2. **Signs** include bilateral optic disc swelling that stabilizes within several months of discontinuing medication.
3. **Visual field defects** may be mild and reversible or severe and permanent.
4. **Prognosis** is variable because cessation of the drug may not bring about improvement.
5. **Screening** is not appropriate because there is no way to identify those at risk. Patients should, however, be warned of the small risk of toxicity and advised to report any suggestive symptoms.

Vigabatrin

Vigabatrin is an antiepileptic drug, used mainly as second-line therapy, except in infantile spasms (West syndrome). A significant percentage of patients develop dyschromatopsia and constricted visual fields when the total dose is 1500 g or more. The defects develop within 1 month and several years of starting therapy and are often permanent despite discontinuation of the drug. Product literature advises visual field testing at six monthly intervals.

Raised intracranial pressure

Introduction

Cerebrospinal fluid

1. **Circulation** (Fig. 18.34a)
   - Cerebrospinal fluid (CSF) is formed by the choroid plexus in the ventricles of the brain.
   - It leaves the lateral ventricles to enter the third ventricle through the foramina of Munro.
   - From the third ventricle, it flows through the sylvian aqueduct to the fourth ventricle.
   - From the fourth ventricle, the CSF passes through the foramina of Luschka and Magendie to enter the subarachnoid space, some flowing around the spinal cord and the rest bathing the cerebral hemispheres.
   - Absorption is into the cerebral venous drainage system through the arachnoid villi.

2. **Normal opening pressure** of CSF on lumbar puncture is <80 mm H_2O in infants, <90 mm in children and <210 mm in adults.

Causes of raised intracranial pressure (Fig. 18.34b)

1. **Obstruction** of the ventricular system by congenital or acquired lesions.
2. **Space-occupying** intracranial lesions, including haemorrhage.
3. **Impairment** of CSF absorption via arachnoid villi, which may be damaged by meningitis, subarachnoid haemorrhage or cerebral trauma.
4. **Idiopathic intracranial hypertension** (pseudo-tumour cerebri).
5. **Diffuse cerebral oedema** from blunt head trauma.
6. **Severe systemic hypertension.**
7. **Hypersecretion of CSF** by choroid plexus tumour, which is very rare.

Hydrocephalus

Hydrocephalus is dilatation of the ventricles (Fig. 18.35). Raised intracranial pressure may be associated with two types of hydrocephalus.

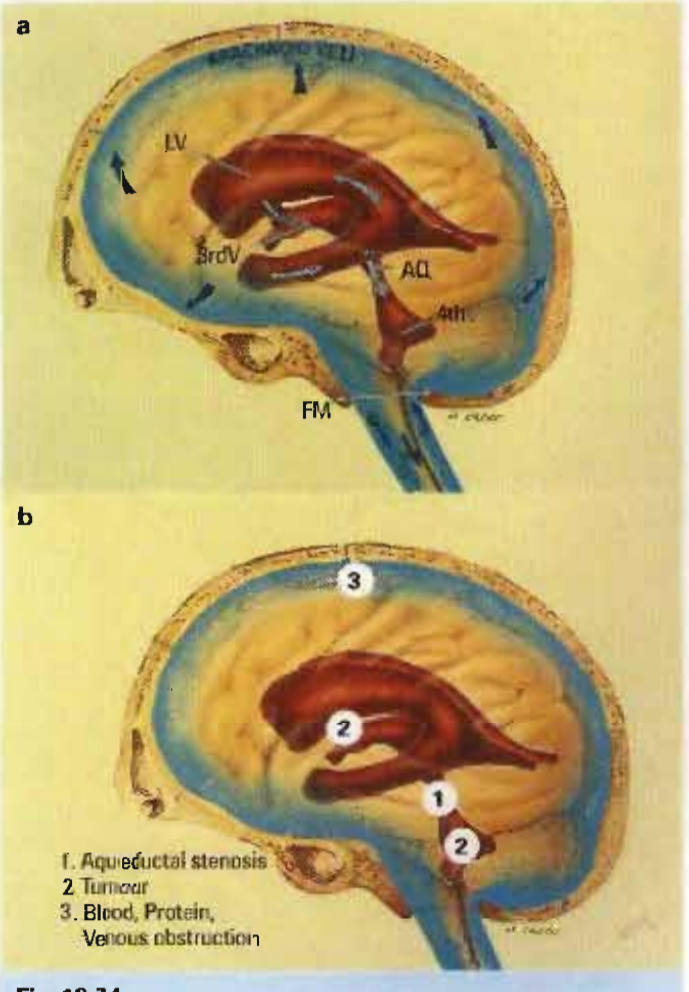


Fig. 18.34
(a) Circulation of cerebrospinal fluid (see *text*); (b) causes of elevation of intracranial pressure (see *text*) (Courtesy of Wilmer Institute)

Fig. 18.35
Axial CT scan showing severe hydrocephalus (Courtesy of K. Nischal)

1. **Communicating hydrocephalus**, in which the CSF flows from the ventricular system to the subarachnoid space without impediment. The obstruction to flow lies in the basilar cisterns or in the subarachnoid space, where there is failure of absorption by the arachnoid villi.
2. **Non-communicating hydrocephalus** is caused by obstruction to CSF flow in the ventricular system or at the exit foramina of the fourth ventricle. The CSF therefore does not have access to the subarachnoid space.

Clinical features

Systemic

1. **Headaches** may come on at any time of day but characteristically occur early in the morning and may wake the patient from sleep. They tend to get progressively worse and patients usually present to hospital within 6 weeks. The headaches may be generalized or localized, and may intensify with head movement, bending or coughing. Patients with lifelong headaches often report a change in character of the headache. Very rarely, headache may be absent.
2. **Sudden nausea and vomiting**, often projectile, may partially relieve the headache. Vomiting may occur as an isolated feature or may precede the onset of headaches by months, particularly in patients with fourth ventricular tumours.
3. **Deterioration of consciousness** may be slight, with drowsiness and somnolence. Dramatic deterioration of consciousness is indicative of brain stem distortion and tentorial or tonsillar herniation and requires prompt attention.

Visual

1. **Transient visual obscurations** lasting a few seconds are frequent in patients with papilloedema.

2. **Horizontal diplopia** is caused by stretching of the sixth nerve over the petrous tip. It is therefore a false localizing sign.
3. **Visual failure** occurs late in patients with secondary optic atrophy due to long-standing papilloedema (*see* below).

Papilloedema

Introduction

By definition, papilloedema is swelling of the optic nerve head, secondary to raised intracranial pressure. It is nearly always bilateral, although it may be asymmetrical. All other causes of disc oedema in the absence of raised intracranial pressure are referred to as 'disc swelling' and usually produce visual impairment. All patients with papilloedema should be suspected of having an intracranial mass unless proved otherwise (Fig. 18.36). However, not all patients with raised intracranial pressure will necessarily develop papilloedema. Tumours of the cerebral hemispheres tend to produce papilloedema later than those in the posterior fossa. Patients with a history of previous papilloedema may develop a substantial increase in intracranial pressure but fail to redevelop papilloedema because of glial scarring of the optic nerve head.

Clinical features

1. **Early papilloedema** (Fig. 18.37) may be difficult to diagnose with certainty. The following are its main features:

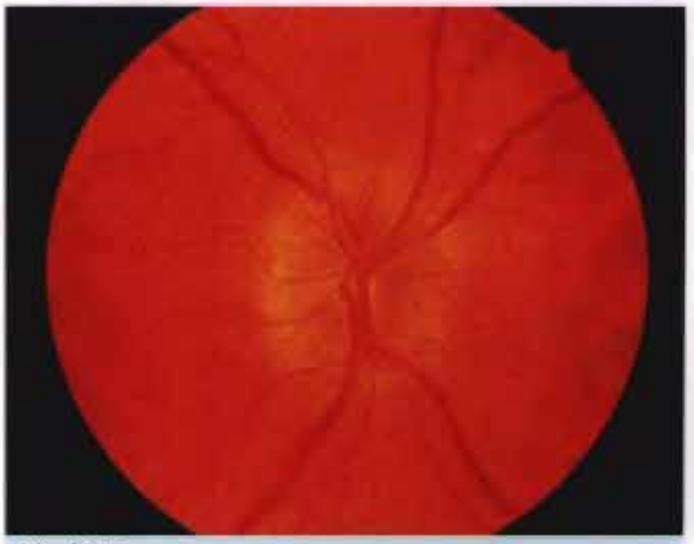


Fig. 18.37
Early papilloedema

- Visual symptoms are absent and visual acuity is normal.
- Optic discs show hyperaemia and mild elevation.
- The disc margins (initially nasal, later superior, inferior and temporal) appear indistinct, and swelling of the parapapillary retinal nerve fibre layer develops.
- There is loss of previous spontaneous venous pulsation. However, as about 20% of normal individuals do not manifest spontaneous venous pulsation, its absence does not necessarily imply raised intracranial pressure.

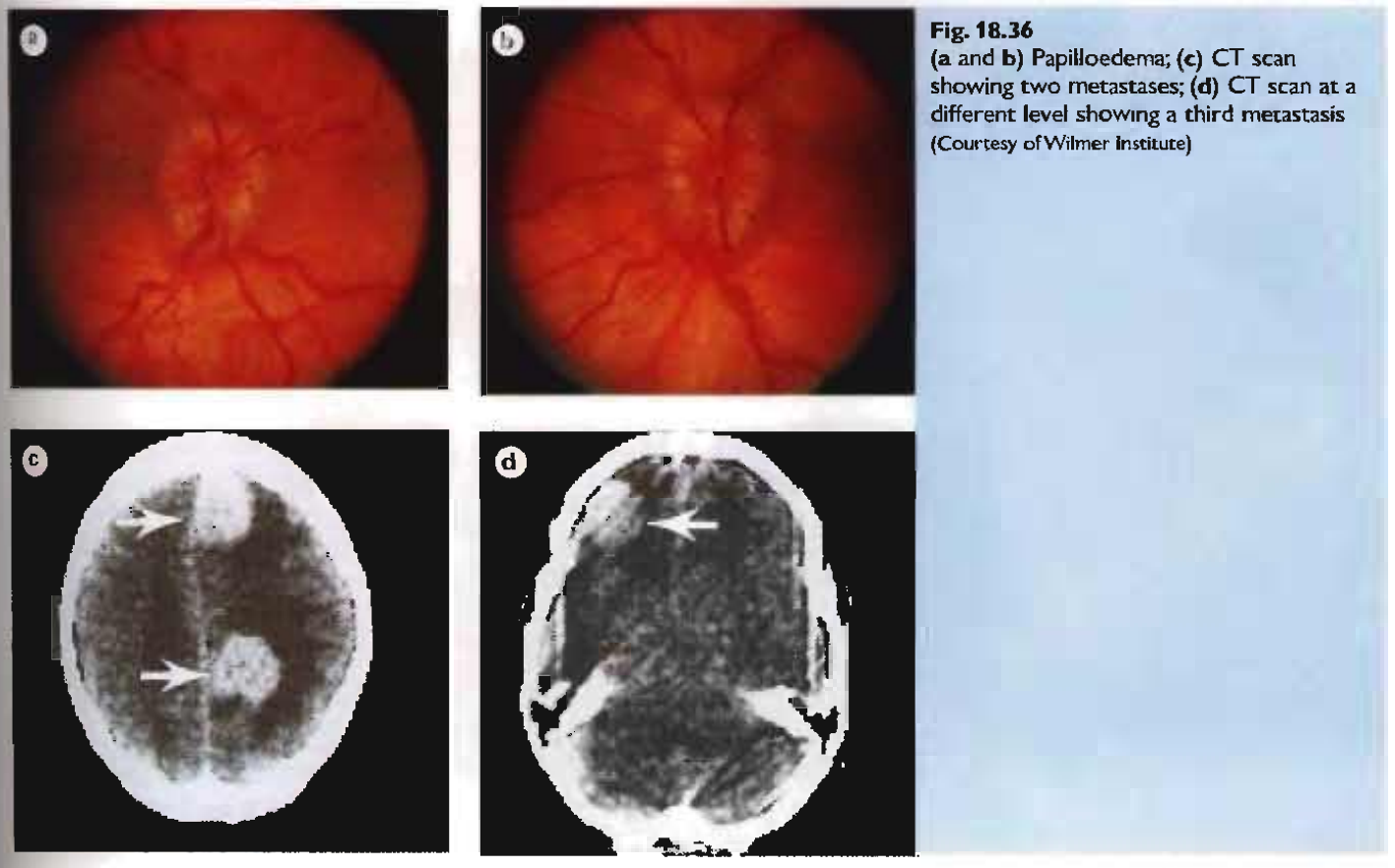


Fig. 18.36
(**a** and **b**) Papilloedema; (**c**) CT scan showing two metastases; (**d**) CT scan at a different level showing a third metastasis
(Courtesy of Wilmer Institute)

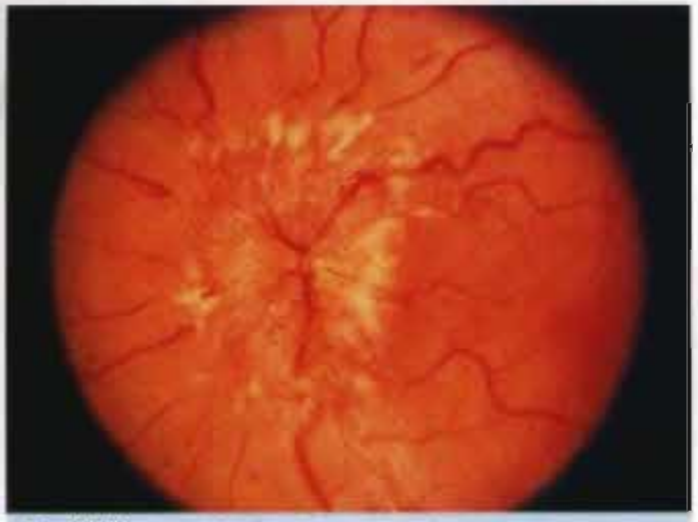


Fig. 18.38
Established papilloedema

Preserved venous pulsation renders the diagnosis of papilloedema unlikely.

2. **Established papilloedema** (Fig. 18.38)
   - Transient visual obscurations may occur in one or both eyes, lasting a few seconds, often on standing.
   - Visual acuity is normal or reduced.
   - Optic discs show severe hyperaemia, and moderate elevation with indistinct margins, which may initially be asymmetrical.
   - The optic cup and the small vessels on the disc are obscured.
   - Venous engorgement, parapapillary flame-shaped haemorrhages and frequently also cotton wool spots may be seen.
   - As the swelling increases, the optic nerve head appears enlarged; circumferential retinal folds may develop on its temporal side.
   - Hard exudates may radiate from the centre of the fovea in the form of a 'macular fan': an incomplete star with the temporal part missing.
   - The blind spot is enlarged.
3. **Long-standing (vintage) papilloedema** (Fig. 18.39)
   - Visual acuity is variable and the visual fields begin to constrict.
   - Optic discs are markedly elevated with a 'champagne cork' appearance.
   - Cotton wool spots and haemorrhages are absent.
   - Opticociliary shunts and drusen-like crystalline deposits (corpora amylacea) may be present on the disc surface.
4. **Atrophic papilloedema (secondary optic atrophy)** (Fig. 18.40)
   - Visual acuity is severely impaired.
   - The optic discs are a dirty grey colour, slightly elevated, with few crossing blood vessels and indistinct margins.

Differential diagnosis

1. **Buried drusen** may be mistaken for early papilloedema (*see* later).
2. **Bilateral disc swelling** may be caused by:
   - Malignant hypertension.
   - Bilateral papillitis.
   - Bilateral compressive thyroid ophthalmopathy.
   - Bilateral simultaneous anterior ischaemic optic neuropathy.
   - Bilaterally compromised venous drainage in central retinal vein occlusion or carotid–cavernous fistula.

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (IIH) deserves special mention, since the ophthalmologist may be involved in

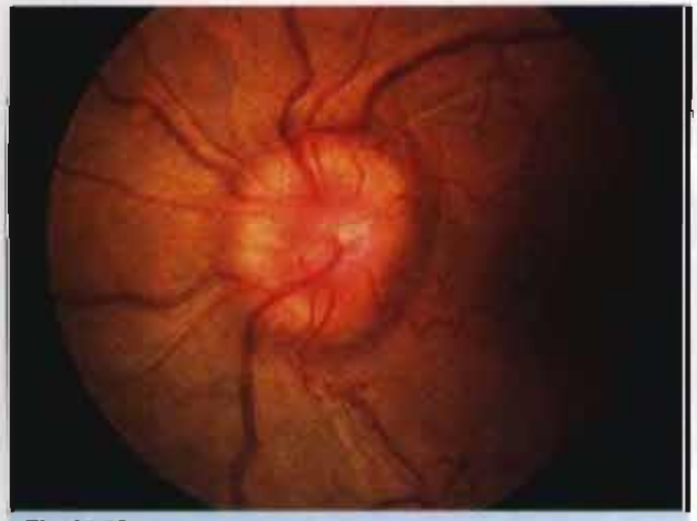


Fig. 18.39
Long-standing papilloedema

Fig. 18.40
Atrophic papilloedema

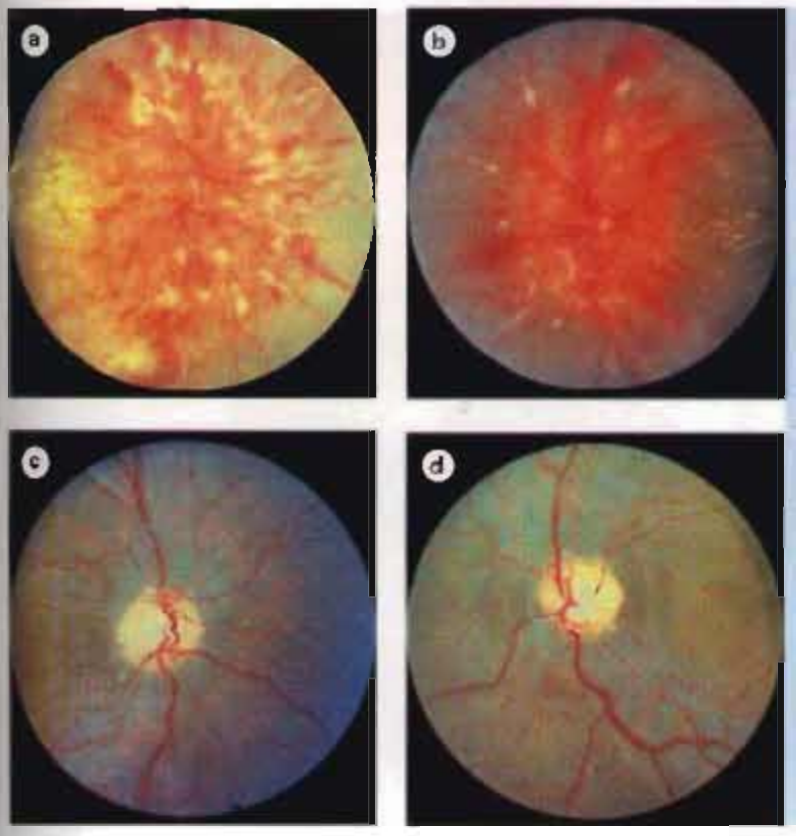


Fig. 18.41
(a and b) Severe papilloedema in idiopathic intracranial hypertension; (c and d) mild optic atrophy following resolution (Courtesy of Wilmer Institute)

management. It is defined as the presence of raised intracranial pressure in the absence of an intracranial mass lesion or enlargement of the ventricles due to hydrocephalus. Although not life-threatening IIH may result in permanent visual damage due to papilloedema. Ninety per cent of patients are obese women of child-bearing age, who are often amenorrhoeic. Intracranial hypertension may also be caused by drugs including tetracyclines, nalidixic acid and iron therapy.

Clinical features

1. **Signs and symptoms** of raised intracranial pressure as described above.
2. **Lumbar puncture** shows an opening pressure of >210 mm H_2O. However, it may be artefactually raised in obese patients with normal intracranial pressure.
3. **Neuroimaging** shows normal or small and slit-like ventricles.
4. **Course.** Most patients have a prolonged course with spontaneous relapses and remissions, although a few may have a short course lasting only a few months. Although mortality is low, visual loss, sometimes severe, is common (Fig. 18.41).

Management

The two main aims are to relieve headaches and to prevent visual loss.

1. **Regular perimetry** is essential to detect early or progressive visual field loss.
2. **Diuretics** such as acetazolamide or thiazides usually relieve headache but their effects on preservation of visual function are unclear.
3. **Systemic steroids** are often used short term but are unsatisfactory for chronic administration because of their potential complications, particularly in obese patients.
4. **Optic nerve fenestration**, which involves incision of the meningeal sheath around the optic nerve, is safe and effective in preserving vision provided it is performed early. However, headache is relieved only in a minority of cases.
5. **Lumboperitoneal shunts** may be performed but the failure rate is high and surgical revision is frequently required.

Congenital optic nerve anomalies with neurological associations

Optic disc drusen

Optic disc drusen (hyaline bodies) are composed of hyaline-like calcific material within the substance of the optic nerve head (Fig. 18.42). Clinically, they are present in about 0.3% of the population and are often bilateral. Although only a minority of family members have disc drusen nearly half

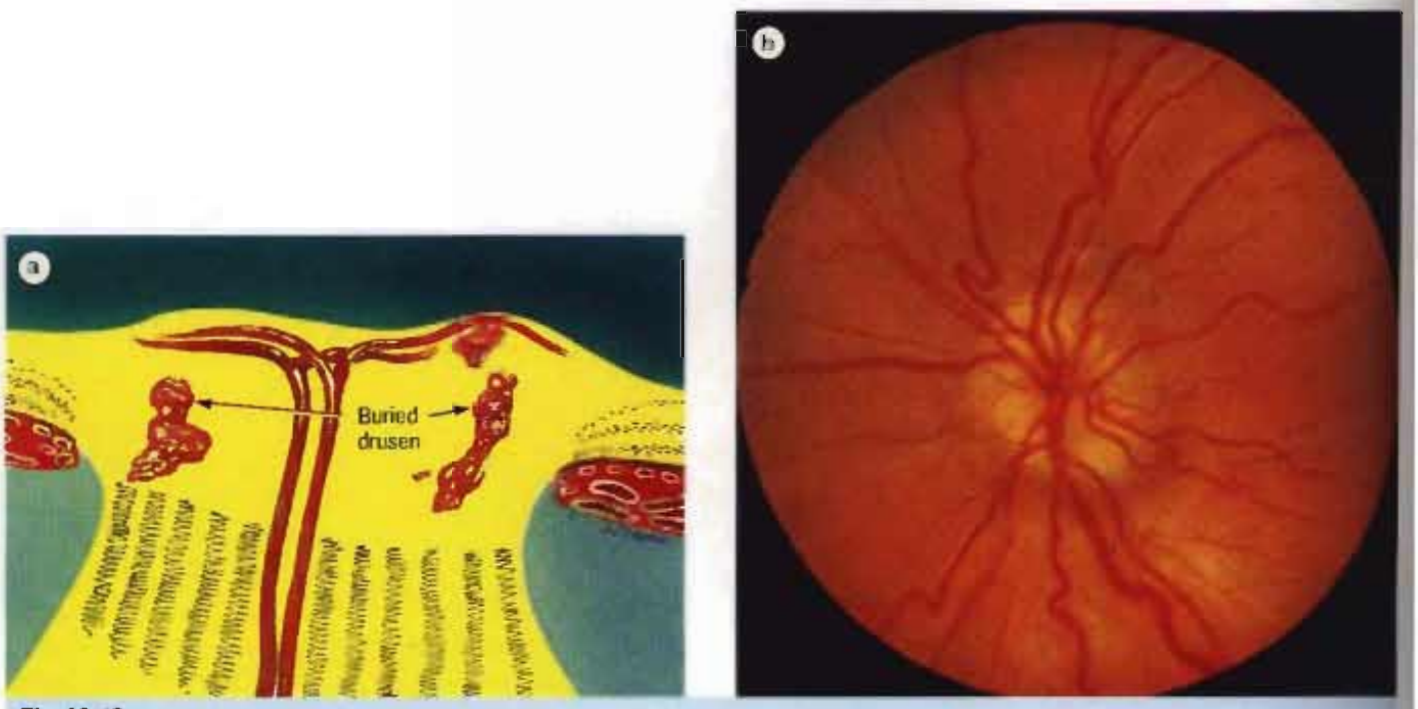


Fig. 18.42
Buried optic disc drusen (see *text*) (Courtesy of Wilmer Institute)

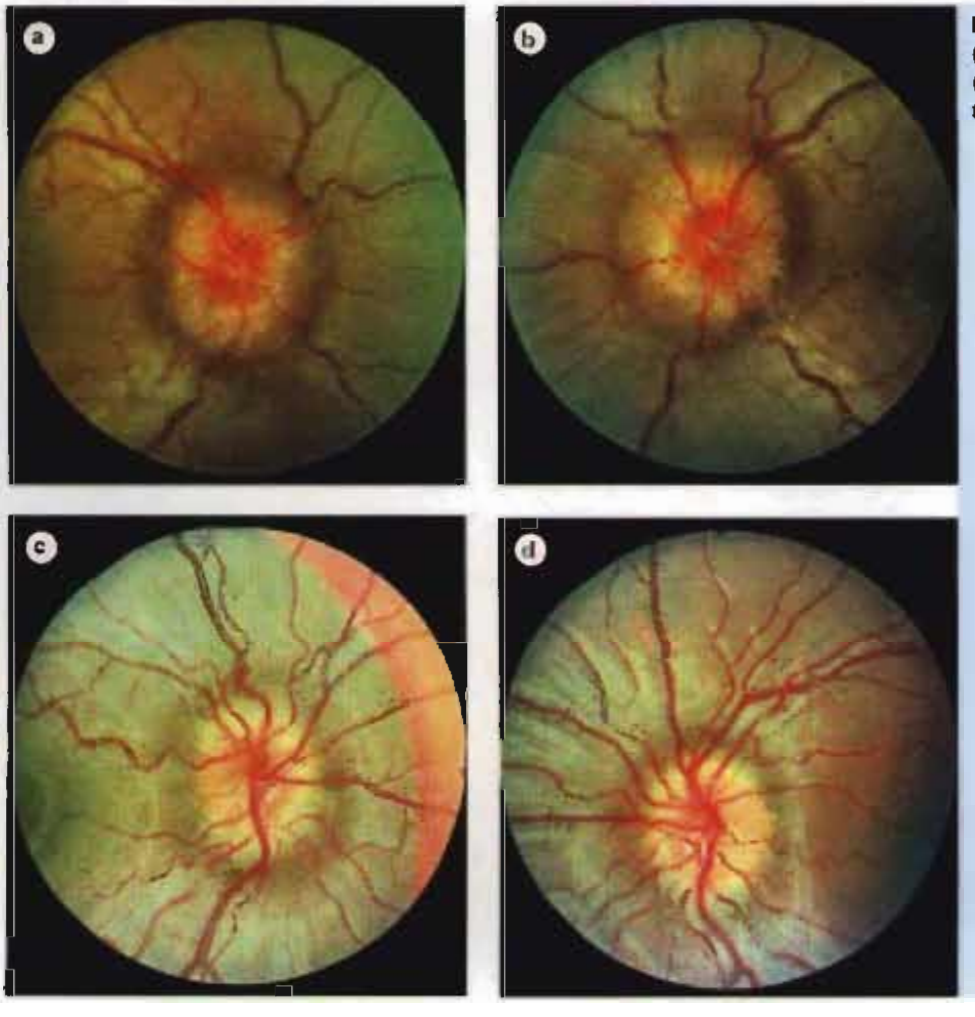


Fig. 18.43
(**a** and **b**) Long-standing papilloedema; (**c** and **d**) buried optic disc drusen (see *text*) (Courtesy of Wilmer Institute)

manifest anomalous disc vessels and absence of the physiological optic cup.

Clinical features

1. **Buried drusen**. In early childhood drusen may be difficult to detect because they lie deep beneath the surface of the disc (Fig. 18.43c and d). In this setting the appearance may mimic papilloedema (Fig. 18.43a and b). Signs suggestive of disc drusen are:
   - Elevated disc with a scalloped margin without a physiological cup.
   - Absence of hyperaemia of the disc surface.
   - The surface vessels are not obscured, despite the disc elevation.
   - Anomalous vascular patterns including early branching, increased number of major retinal vessels and vascular tortuosity.
   - Spontaneous venous pulsation may be present in 80% of cases.
2. **Exposed drusen**. During the early teens drusen usually emerge at the surface of the disc as waxy pearl-like irregularities (Fig. 18.44).
3. **Complications** are uncommon.
   - A small minority of patients develop visual impairment as a result of juxtapapillary choroidal neovascularization (Fig. 18.45).
   - Occasionally a progressive but limited loss of visual field with a nerve fibre bundle pattern may occur.
4. **Associations** include retinitis pigmentosa, angioid streaks and Allagille syndrome.

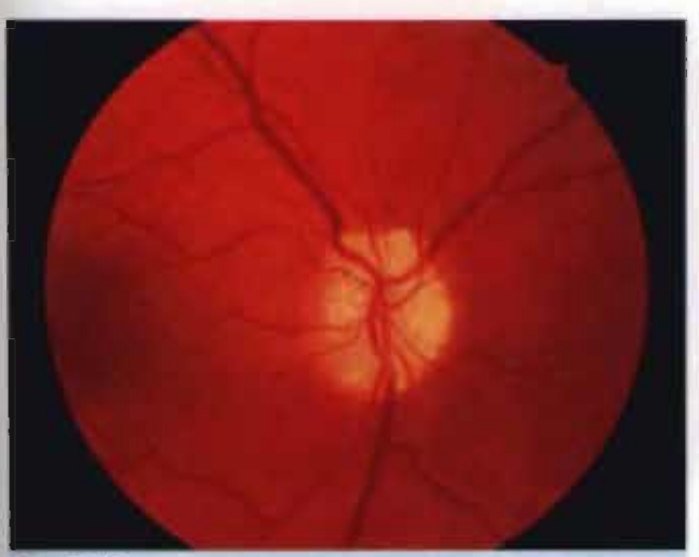


Fig. 18.44
Exposed optic disc drusen

Special investigations

The following may be necessary for the definitive diagnosis of disc drusen, particularly when buried:

1. **Ultrasonography** (Fig. 18.46) is the most readily available and reliable method because of its ability to detect calcific deposits. With the gain turned down, drusen can still be recognized by their high acoustic reflectivity.
2. **CT** (Fig. 18.47) is less sensitive than ultrasonography and may miss small drusen. Drusen may, however, be detected incidentally on CT, when performed in the course of investigation of other pathology.

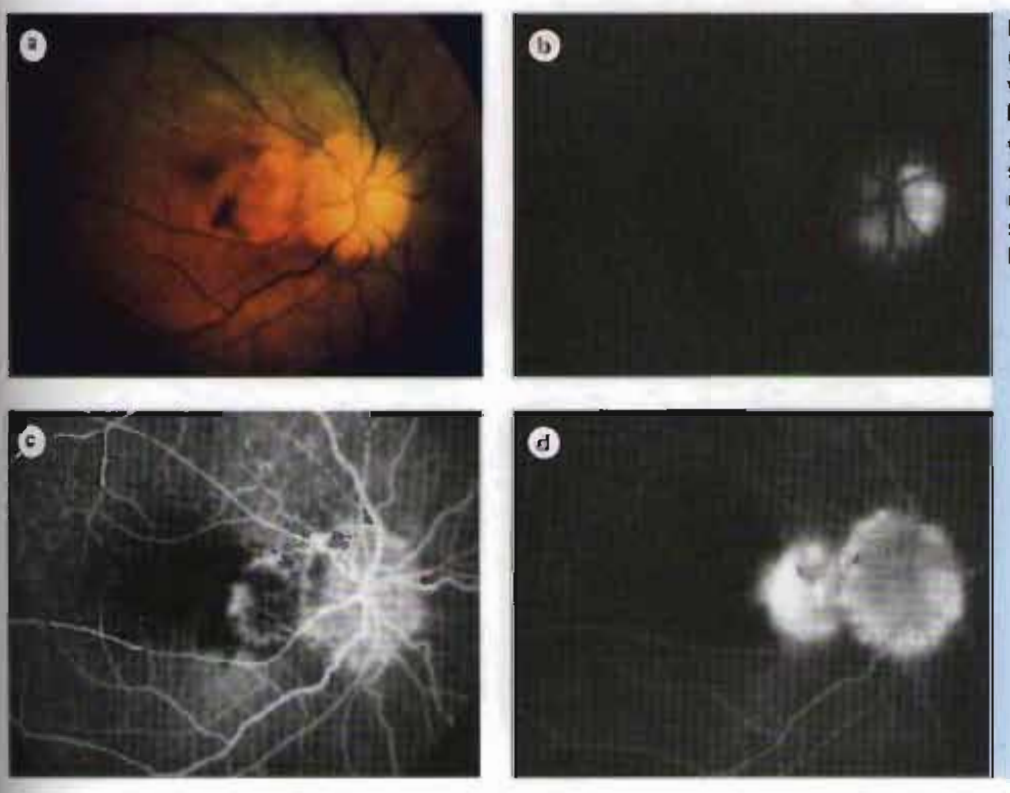


Fig. 18.45
(a) Optic disc drusen associated with macular oedema and haemorrhage; (b) autofluorescence of drusen; (c) early venous phase FA showing parapapillary choroidal neovascularization; (d) late phase showing hyperfluorescence due to leakage (Courtesy of S. Milewski)

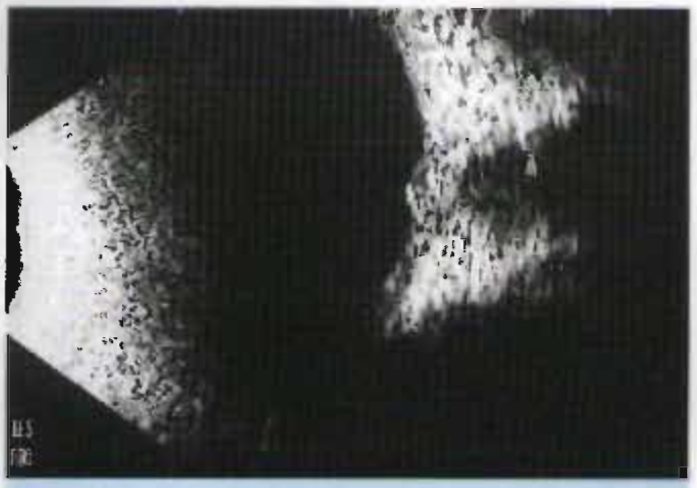


Fig. 18.46
B scan ultrasonogram of optic disc drusen

Fig. 18.47
Axial CT scan of optic disc drusen

3. **FA** may occasionally be helpful and shows the following:
   - Exposed drusen (Fig. 18.48a and b) show the phenomenon of autofluorescence prior to dye injection (Fig. 18.48c) and late localized hyperfluorescence due to staining (Fig. 18.48d). However, these phenomena may not be prominent with buried drusen because of attenuation from the overlying tissue (Fig. 18.49).

NB: FA in papilloedema shows increasing hyperfluorescence and late leakage (Fig. 18.50).

Optic disc coloboma

An optic disc coloboma results from incomplete closure of the choroidal fissure. It is a rare condition, mostly sporadic, although AD inheritance may occur. Optic disc colobomas occur unilaterally or bilaterally with equal frequency and may have profound systemic implications.

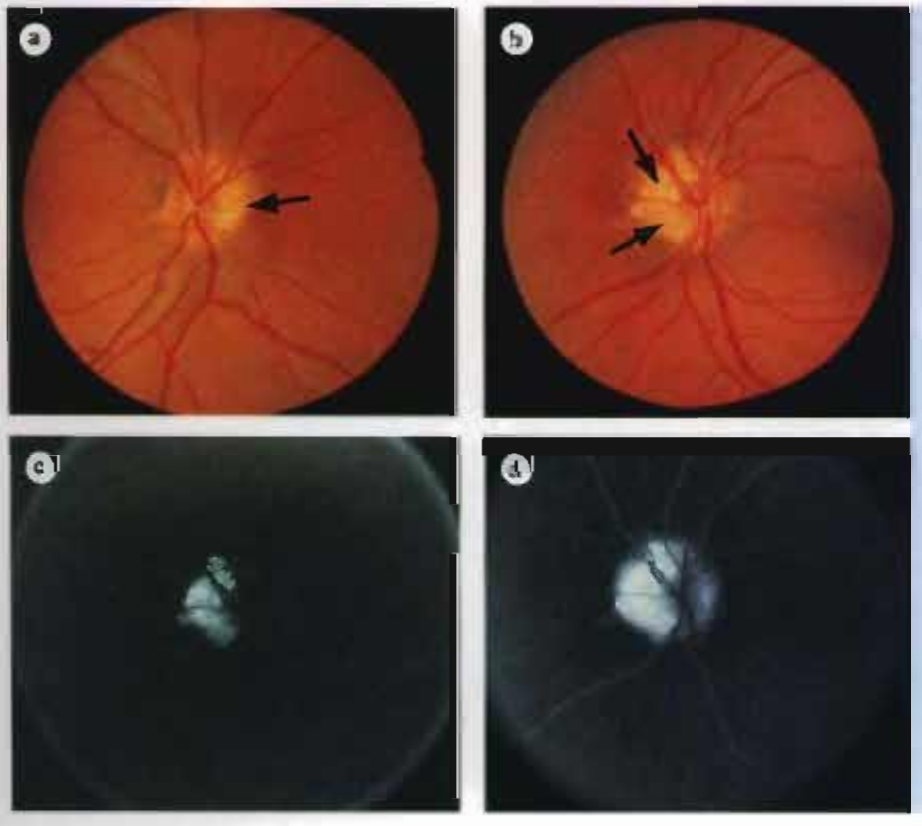


Fig. 18.48
(a and b) Exposed optic disc drusen; (c) autofluorescence; (d) late phase FA showing marked hyperfluorescence confined to the disc due to staining without leakage
(Courtesy of Wilmer Eye Institute)

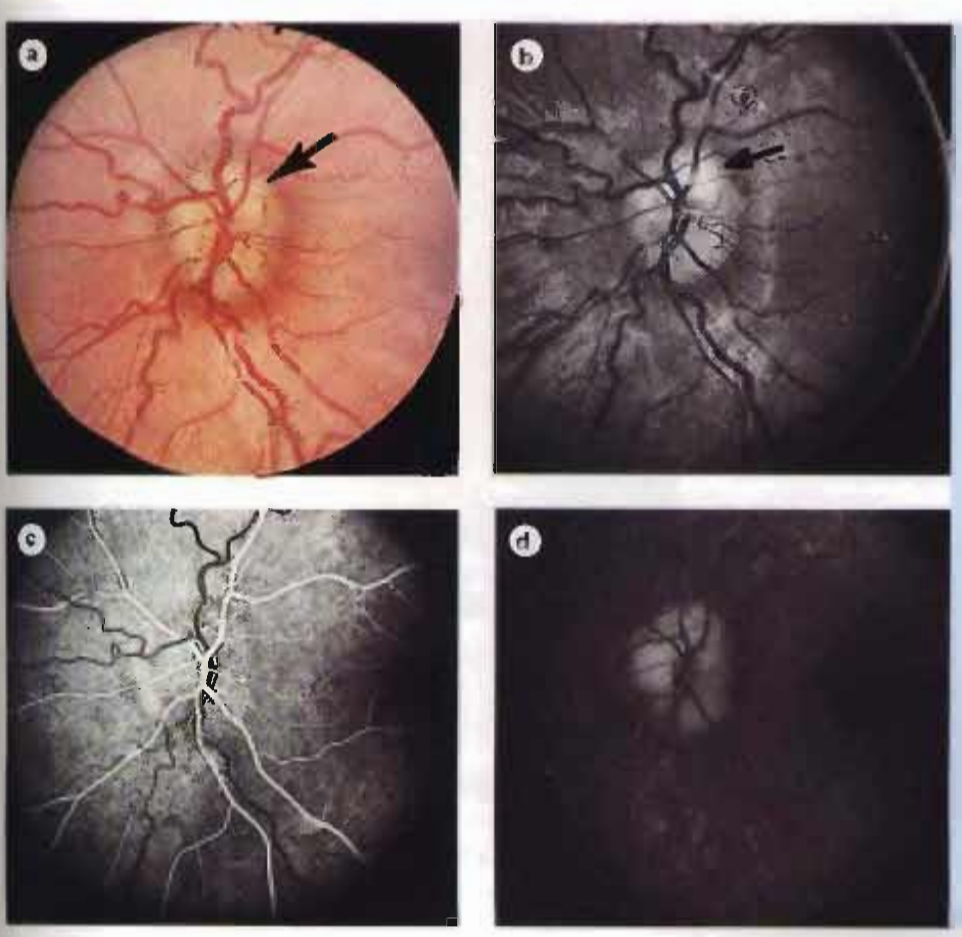


Fig. 18.49
(a) Buried optic disc drusen (arrow); (b) red-free photograph; (c) arterial phase FA is normal; (d) late phase showing mild hyperfluorescence confined to the disc (Courtesy of Wilmer Institute)

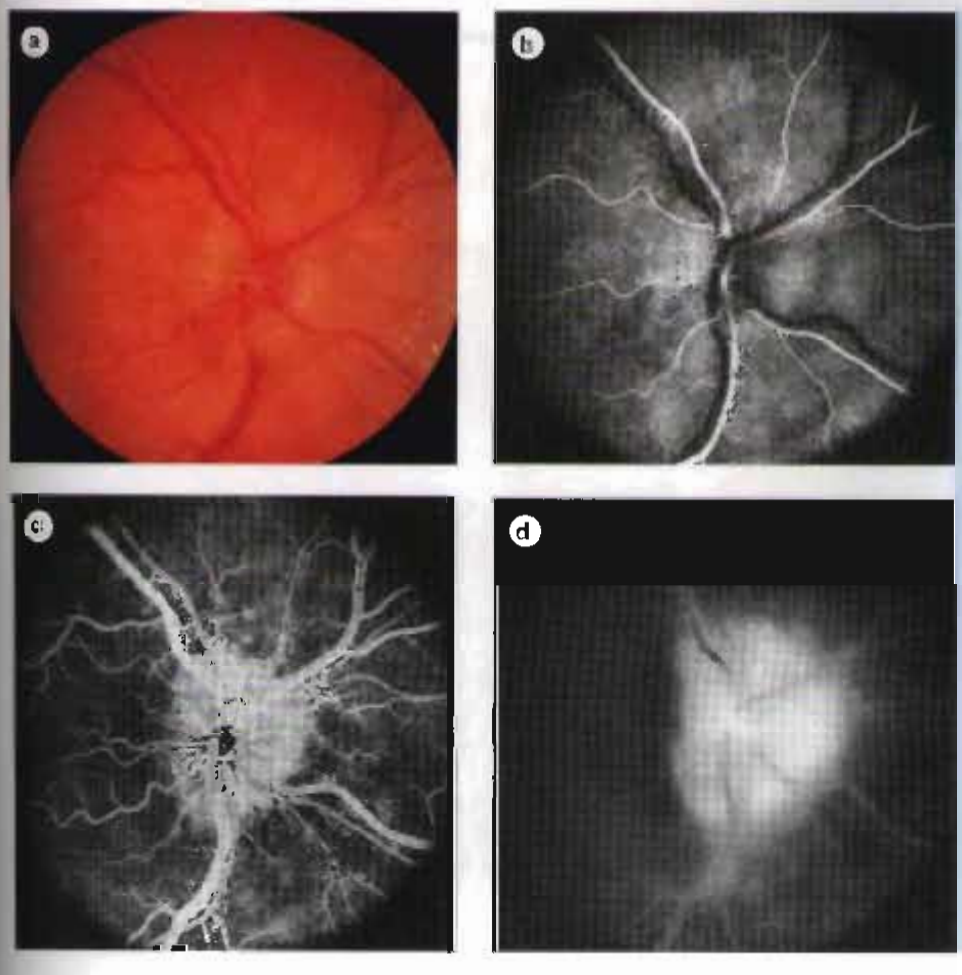


Fig. 18.50
(a) Papilloedema; (b) arterial phase FA showing congested parapapillary capillaries along the retinal nerve fibre layer; (c) arteriovenous phase showing increased hyperfluorescence of dilated capillaries extending to adjacent retina; (d) late phase showing marked hyperfluorescence due to leakage (Courtesy of A. Chopdar)

Clinical features

1. **Signs**
   - Visual acuity is often decreased.
   - The disc shows a discrete, focal, glistening, white, bowl-shaped excavation, decentred inferiorly so that the inferior neuroretinal rim is thin or absent and normal disc tissue is confined to a small superior wedge (Fig. 18.51a).
   - The optic disc itself may be enlarged.
   - Retinal vasculature is normal.
2. **Visual fields** show a superior defect (Fig. 18.51b) which, in conjunction with the disc appearance, may be mistaken for normal-tension glaucoma.
3. **Ocular associations** include microphthalmos and colobomas of iris (*see* Fig. 18.54), ciliary body and fundus (Fig. 18.52).
4. **Complications**
   - Serous retinal detachment at the macula may occur (*see* Fig. 18.51a).
   - Progressive enlargement of the excavation and neural rim thinning despite normal intraocular pressure has been described.
   - Rhegmatogenous retinal detachment may occur in eyes with associated chorioretinal colobomas.

Systemic associations

These are numerous. Only the most important will be mentioned.

1. **Chromosomal anomalies** include Patau syndrome (trisomy 13), Edward syndrome (trisomy 18) and Cat-eye syndrome (trisomy 22).
2. **'CHARGE'** association comprises Coloboma, Heart defects, choanal Atresia, Retarded growth and development, Genital and Ear anomalies.

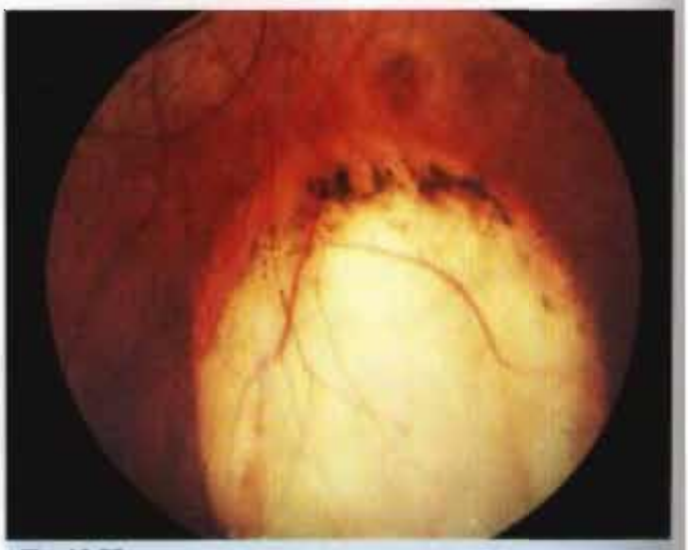


Fig. 18.52
Chorioretinal coloboma

3. **Other syndromes** include Meckel–Gruber, Goltz, Lenz microphthalmos, Walker–Warburg, Goldenhar, Dandy–Walker cyst and Rubinstein–Taybi.

Morning glory anomaly

Morning glory anomaly is a very rare, usually unilateral sporadic condition. Bilateral cases, which are rarer still, may be hereditary.

Clinical features

1. **Signs**
   - Visual acuity is usually very poor.
   - The disc is enlarged and manifests a funnel-shaped excavation (Fig. 18.53).

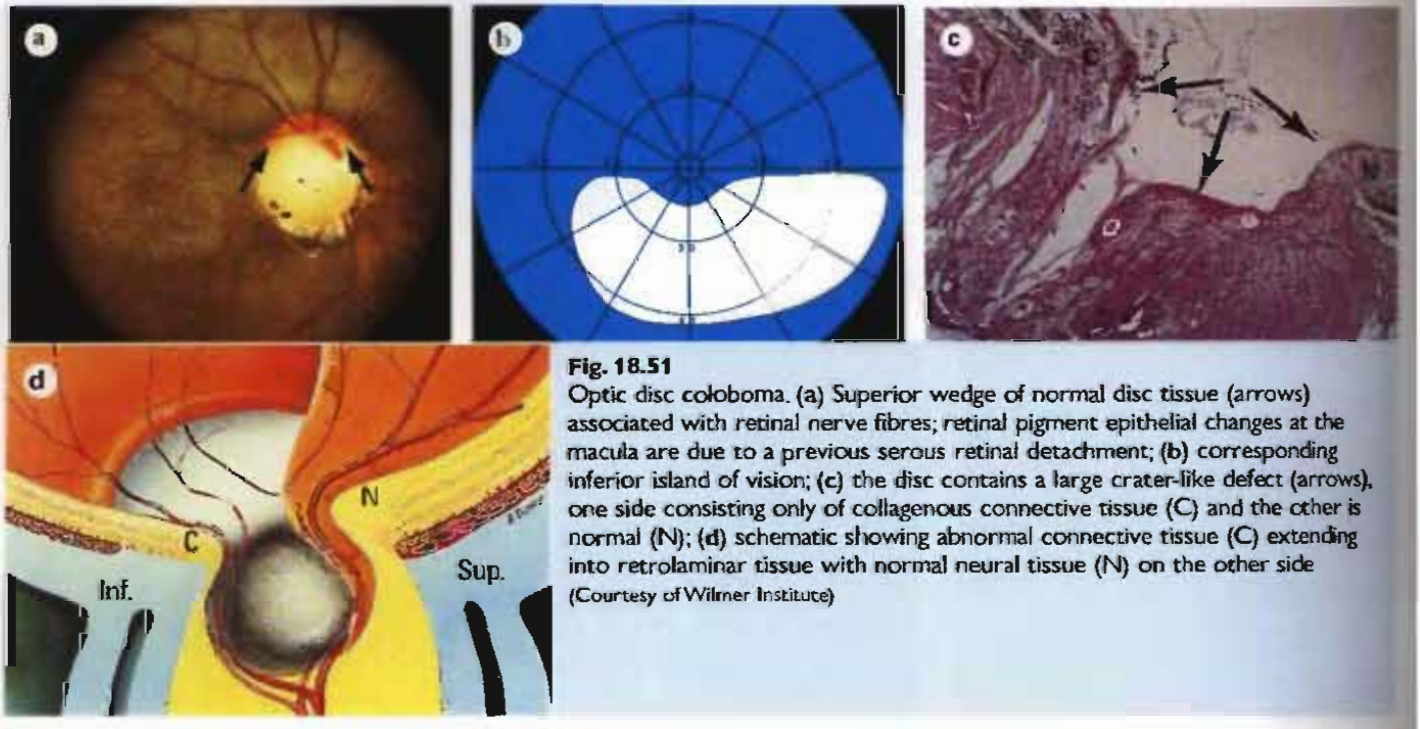


Fig. 18.51
Optic disc coloboma. (a) Superior wedge of normal disc tissue (arrows) associated with retinal nerve fibres; retinal pigment epithelial changes at the macula are due to a previous serous retinal detachment; (b) corresponding inferior island of vision; (c) the disc contains a large crater-like defect (arrows), one side consisting only of collagenous connective tissue (C) and the other is normal (N); (d) schematic showing abnormal connective tissue (C) extending into retrolaminar tissue with normal neural tissue (N) on the other side
(Courtesy of Wilmer Institute)

- A central core of whitish glial tissue, representing persistent hyaloid remnants lies at the base of the excavation.
- The disc is surrounded by an elevated annulus of chorioretinal pigmentary disturbance.
- The blood vessels emerge from the rim of the excavation in a radial pattern like the spokes of a wheel. They are increased in number and it is difficult to distinguish arteries from veins.

2. **Complication**. Serous retinal detachment develops in about 30% of cases.

Systemic associations

Uncommon systemic associations include the following:

1. **Frontonasal dysplasia**, the most important, is characterized by a malformation complex consisting of:
   - Mid-facial anomalies including hypertelorism, depressed nasal bridge (Fig. 18.54) hare lip and cleft palate.
   - Basal encephalocele (Figs 18.55 and 18.56), absent corpus callosum and pituitary deficiency.
2. **Neurofibromatosis type 2** is a rare association.

Optic nerve hypoplasia

The hypoplastic optic nerve, unilateral or bilateral, is characterized by a diminished number of nerve fibres. It may occur as an isolated anomaly in an otherwise normal eye, in a grossly malformed eye or in association with a heterogeneous group of disorders most commonly involving the midline structures of the brain. Specific agents used by the mother during gestation which may be associated with optic nerve hypoplasia include alcohol, LSD, quinine, protamine zinc insulin, steroids, diuretics, cold remedies and anticonvulsants. Superior segmental hypoplasia may be associated with maternal diabetes.

Clinical features

1. **Signs**
   - Visual acuity can vary from normal to no light perception.

Fig. 18.54
A patient with iris colobomas, hypertelorism and a depressed nasal bridge

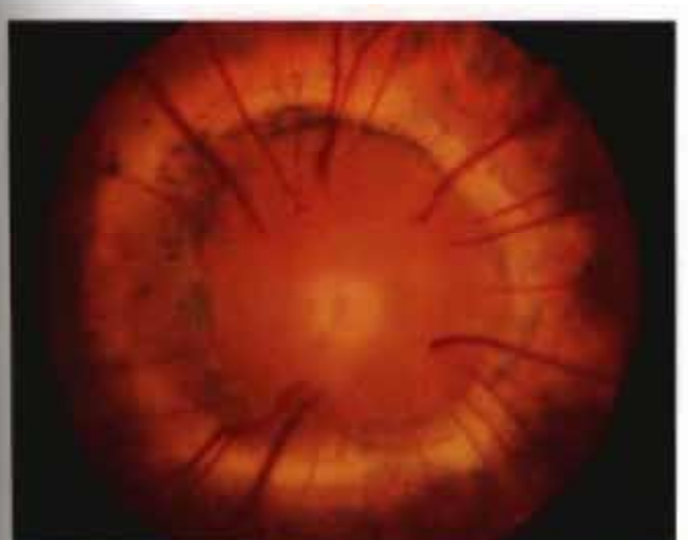


Fig. 18.53
Morning glory anomaly

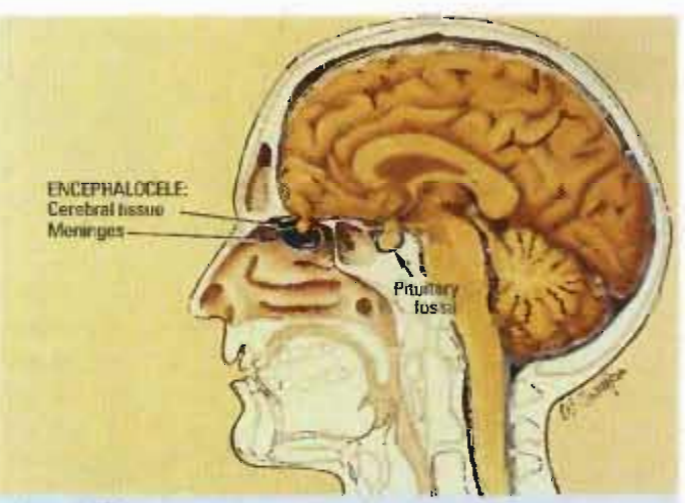


Fig. 18.55
Basal encephalocele (Courtesy of Wilmer Institute)

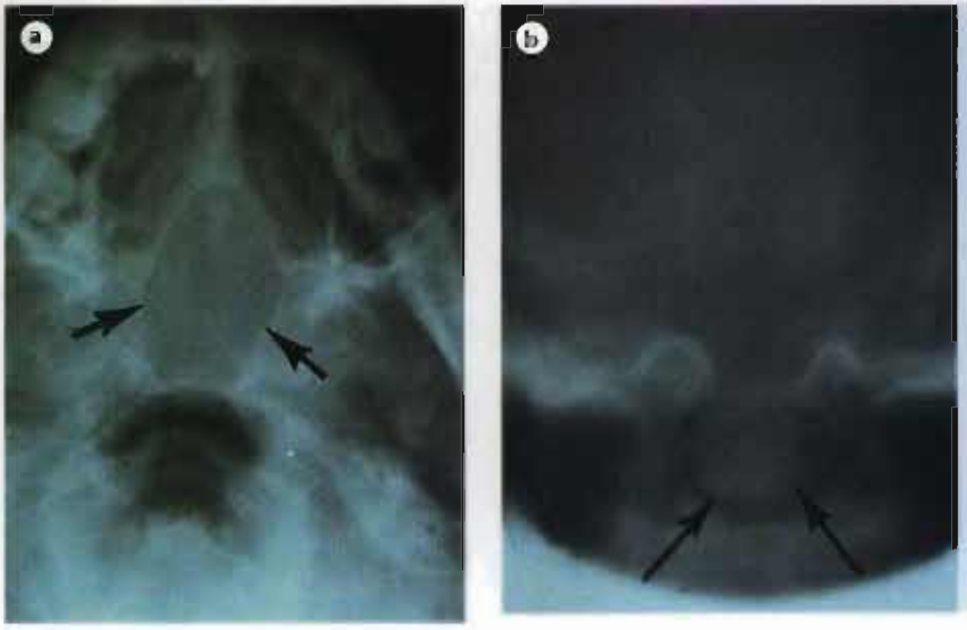
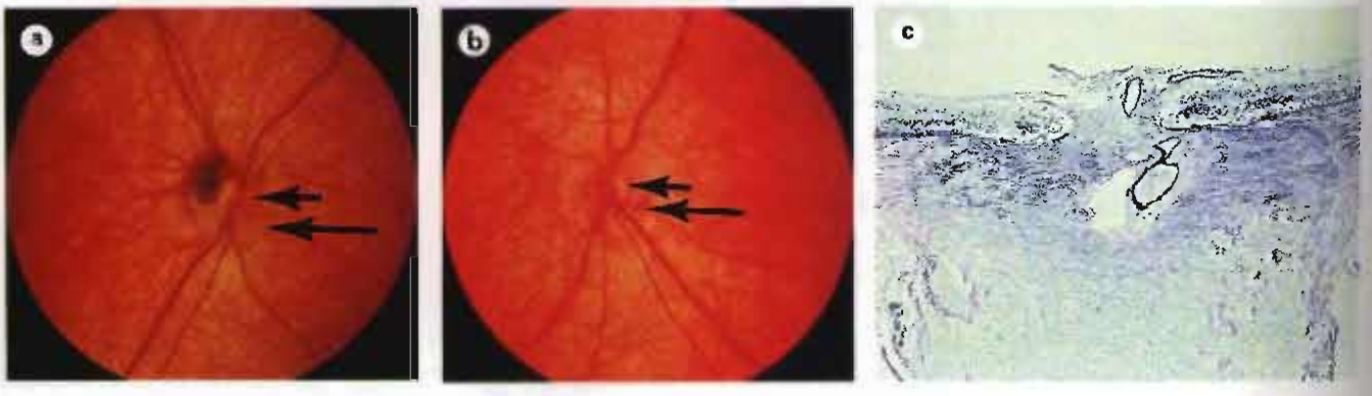


Fig. 18.56
Basal encephalocele. (a) Defect on the bony floor of the skull (arrows); (b) soft tissue protruding through the defect (arrows) (Courtesy of Wilmer Institute)



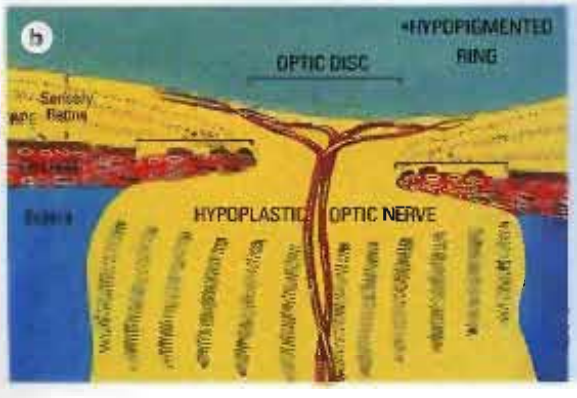


Fig. 18.57
Optic nerve hypoplasia. (a and b) Disc outline (short arrow), hypopigmented ring (long arrow); (c) longitudinal section showing hypoplasia of the disc and retrolaminar optic nerve; (d) hypopigmented ring due to absence of the retinal pigment epithelium (Courtesy of Wilmer Institute)

- The disc is small and grey and is surrounded by a yellow halo of hypopigmentation caused by concentric chorioretinal atrophy (double-ring sign) (Fig. 18.57). The outer ring represents what would have been the normal disc margin.
- The distance from the fovea to the temporal border of the optic disc often equals or exceeds three times the disc diameter. This strongly suggests disc hypoplasia.
- Despite the small size of the disc, the retinal blood vessels are of normal calibre, although they may be tortuous.
- In some cases only a part of the disc is hypoplastic (Fig. 18.58).

2. **Other features** vary considerably, depending on the severity. They include field defects, dyschromatopsia, afferent pupillary defect, foveal hypoplasia, aniridia, microphthalmos, strabismus and nystagmus in severe bilateral cases. Mild cases can be easily overlooked; the slight reduction of visual acuity may be mistaken for amblyopia and treated by occlusion.

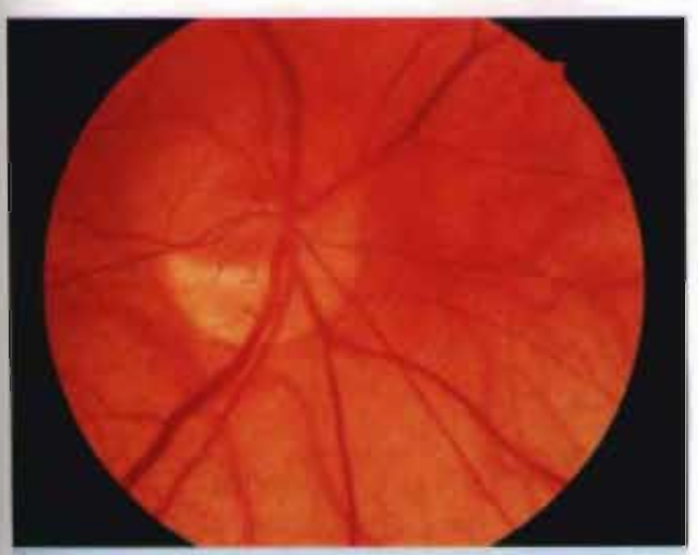


Fig. 18.58
Sectoral optic disc hypoplasia

Systemic associations

1. **de Morsier syndrome** (septo-optic dysplasia) is present in about 10% of cases. In addition to bilateral optic nerve hypoplasia (Fig. 18.59a and b), this involves a spectrum of midline developmental brain defects which may or may not be associated with endocrine abnormalities. These defects include absence or dysgenesis of the septum pellucidum (Fig. 18.59c), thinning or agenesis of the corpus callosum (Fig. 18.60), dysplasia of the anterior third ventricle. Hypopituitarism with low growth hormone levels is common and if recognized early, the deficiency can be corrected and normal growth resumed. It has been suggested that retinal venous tortuosity in patients with bilateral optic nerve hypoplasia may be a marker for potential endocrine dysfunction.
2. **Frontonasal dysplasia** (*see* above) is an occasional association.

Aicardi syndrome

Aicardi syndrome is a very rare X-linked dominant disorder which is lethal *in utero* for males. Ocular involvement is usually bilateral but often asymmetrical.

1. **Signs**
   - Multiple depigmented 'chorioretinal lacunae' clustered around the disc are pathognomonic (Fig. 18.61).
   - Congenital disc anomalies include coloboma, hypoplasia and pigmentation.
2. **Other ocular features** include microphthalmos, persistent pupillary membranes, cataract and iris colobomas.
3. **Systemic features** include infantile spasms, agenesis of the corpus callosum, skeletal malformations and psycho-

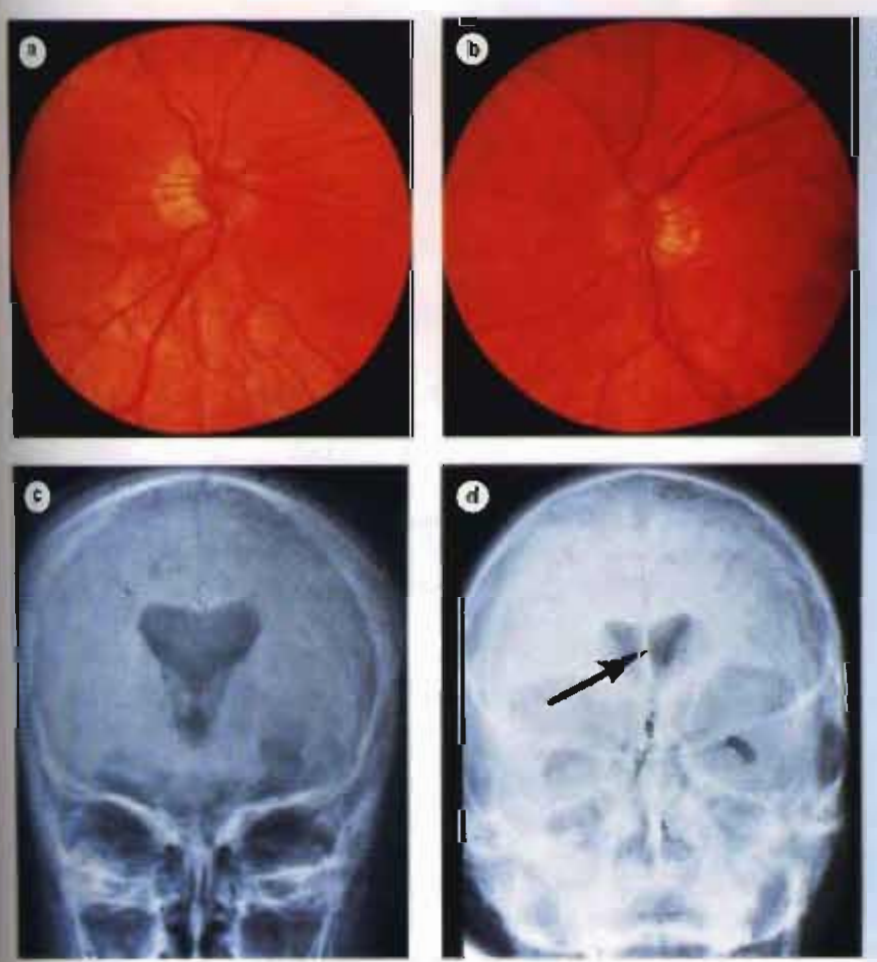


Fig. 18.59
de Morsier syndrome. (a and b) Optic disc hypoplasia; (c) absence of the septum pellucidum; (d) normal septum pellucidum (arrow) for comparison (Courtesy of Wilmer Institute)

Fig. 18.60
Sagittal MRI scan showing absence of the corpus callosum
(Courtesy of K. Nischal)

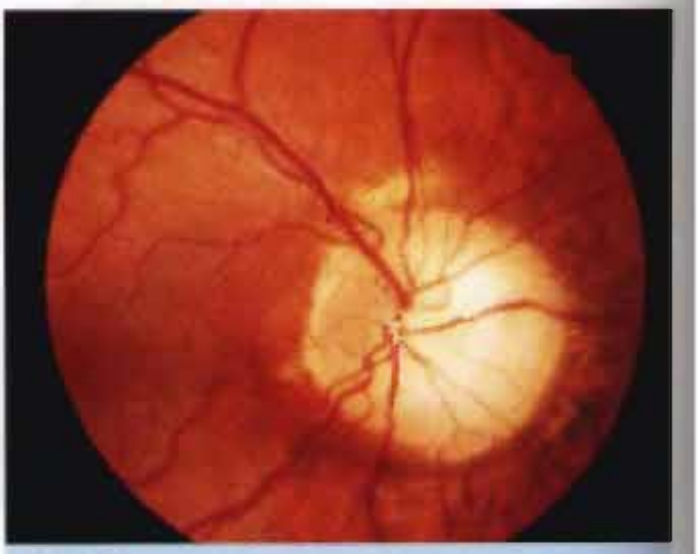


Fig. 18.62
Megalopapilla

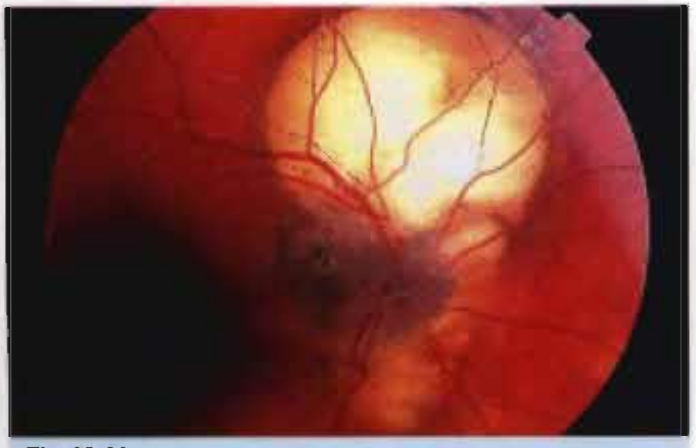


Fig. 18.61
Anomalous optic disc and chorioretinal lacunae in Aicardi syndrome

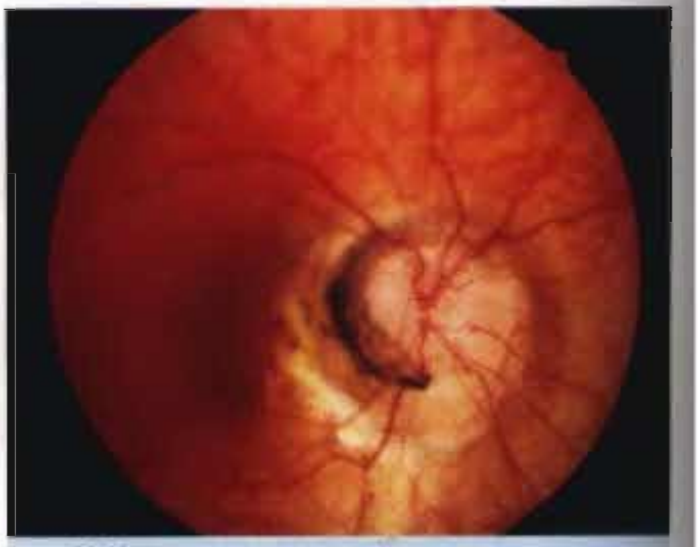


Fig. 18.63
Parapapillary staphyloma

motor retardation. Other serious CNS malformations may also be present and death usually occurs within the first few years of life.

Other anomalies

Miscellaneous rare optic disc anomalies which occasionally have neurological associations include the following:

1. **Megalopapilla**, in which the horizontal and vertical disc diameters are 2.1 mm or more (Fig. 18.62).
2. **Parapapillary staphyloma** is a non-hereditary, usually unilateral condition in which a relatively normal disc sits at the base of a deep excavation whose walls, as well as the surrounding choroid and retinal pigment epithelium, show atrophic changes (Fig. 18.63). Visual acuity is markedly reduced and local retinal detachment may be present. Frontonasal dysplasia is an occasional association.
3. **Optic disc dysplasia** is a descriptive term for a markedly deformed disc that does not conform to any recognizable category (Fig. 18.64).

Pupillary reactions

Applied anatomy

Light reflex

The light reflex is mediated by the retinal photoreceptors and subserved by four neurones (Fig. 18.65).

Fig. 18.64
Dysplastic disc (Courtesy of C. Barry)

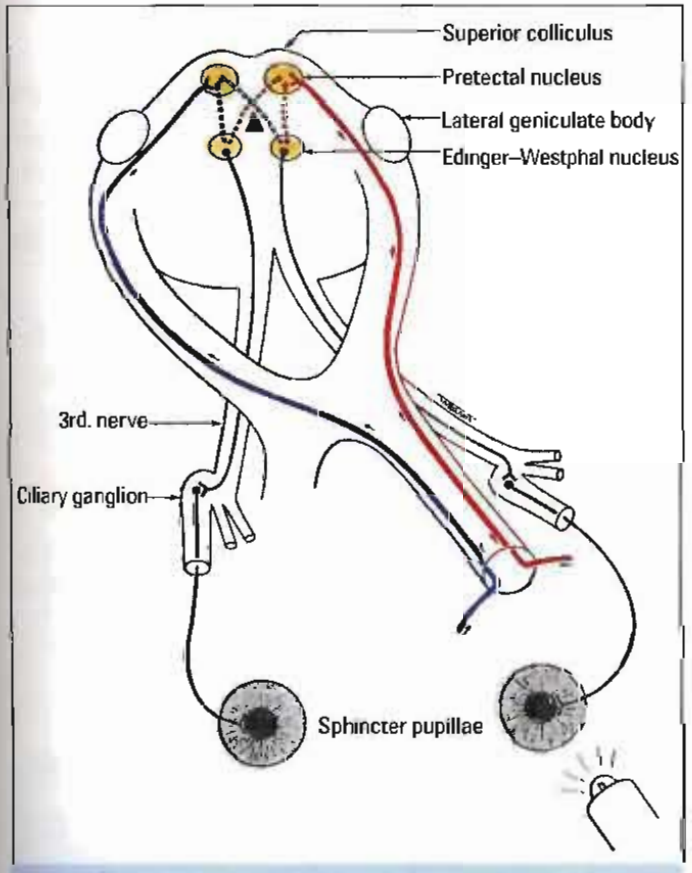


Fig. 18.65
Anatomical pathway of the pupillary light reflex

1. **The first** (sensory) connects each retina with both pretectal nuclei in the midbrain at the level of the superior colliculi. Impulses originating from the nasal retina are conducted by fibres which decussate in the chiasm and pass up the opposite optic tract to terminate in the contralateral pretectal nucleus. Impulses originating in the temporal retina are conducted by uncrossed fibres (ipsilateral optic tract) which terminate in the ipsilateral pretectal nucleus.
2. **The second** (internuncial) connects each pretectal nucleus to both Edinger–Westphal nuclei. Thus a uniocular light stimulus evokes bilateral and symmetrical pupillary constriction. Damage to these internuncial neurones is responsible for light-near dissociation in neurosyphilis and pinealomas.
3. **The third** (preganglionic motor) connects the Edinger–Westphal nucleus to the ciliary ganglion. The parasympathetic fibres pass through the oculomotor nerve, enter its inferior division and reach the ciliary ganglion via the nerve to the inferior oblique muscle.
4. **The fourth** (postganglionic motor) leaves the ciliary ganglion and passes in the short ciliary nerves to innervate the sphincter pupillae. The ciliary ganglion is located within the muscle cone, just behind the globe. It should be noted that, although the ciliary ganglion serves as a conduit for other nerve fibres, only the parasympathetic fibres synapse there.

Near reflex

The near reflex, a synkinesis rather than a true reflex, is activated when gaze is changed from a distant to a near target. It comprises accommodation, convergence and miosis. Vision is not a prerequisite for the near reflex, and there is no clinical condition in which the light reflex is present but the near response absent. Although the final pathways for the near and light reflexes are identical (i.e. third nerve, ciliary ganglion, short ciliary nerves), the centre for the near reflex is ill-defined. There are probably two supranuclear influences: the frontal and occipital lobes. The midbrain centre for the near reflex is probably located more ventrally than the pretectal nucleus and this may explain why compressive lesions such as pinealomas preferentially involve the dorsal internuncial neurones involved in the light reflex, sparing the ventral (near reflex) fibres until later.

Sympathetic innervation

The sympathetic supply involves three neurones (Fig. 18.66):

1. **The first** (central) starts in the posterior hypothalamus and descends, uncrossed, down the brain stem to terminate in the ciliospinal centre of Budge, in the intermediolateral horn of the spinal cord, located between C8 and T2.
2. **The second** (preganglionic) passes from the ciliospinal centre to the superior cervical ganglion in the neck. During its long course, it is closely related to the apical pleura, where it may be damaged by bronchogenic carcinoma (Pancoast tumour) or during surgery on the neck.
3. **The third** (postganglionic) ascends along the internal carotid artery to enter the cavernous sinus where it joins the ophthalmic division of the trigeminal nerve. The sympathetic fibres reach the ciliary body and the dilator pupillae muscle via the nasociliary nerve and the long ciliary nerves.

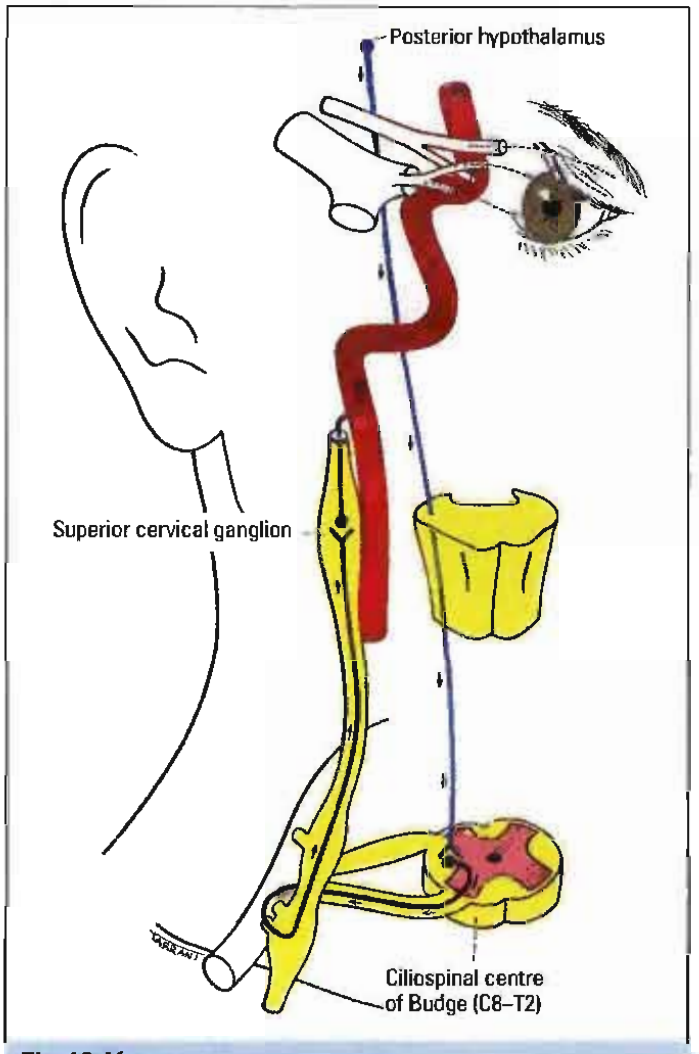


Fig. 18.66
Anatomical pathway of the sympathetic nerve supply

Afferent pupillary defects

Absolute afferent pupillary defect

An absolute afferent pupillary defect (amaurotic pupil) is caused by a complete optic nerve lesion and is characterized by the following:

- The involved eye is completely blind (i.e. no light perception).
- Both pupils are equal in size.
- When the affected eye is stimulated by light neither pupil reacts but when the normal eye is stimulated both pupils react normally.
- The near reflex is normal in both eyes.

Relative afferent pupillary defect

A relative pupillary defect (Marcus Gunn pupil) is caused by an incomplete optic nerve lesion or severe retinal disease, but never by a dense cataract. The clinical features are those of an amaurotic pupil but more subtle. Thus the pupils respond weakly to stimulation of the diseased eye and briskly to that of the normal eye. The difference between the pupillary reactions of the two eyes is highlighted by the '*swinging-flashlight test*' in which a light source is alternatively switched from one eye to the other and back, thus stimulating each eye in rapid succession. First the normal eye is stimulated, resulting in brisk constriction of both pupils. Then when the light is swung to the diseased eye, both pupils dilate instead of constricting. This paradoxical dilatation of the pupils in response to light occurs because the dilatation produced by withdrawing the light from the normal eye outweighs the constriction produced by stimulating the abnormal eye.

> ***NB:*** In afferent (sensory) lesions, the pupils are equal in size. Anisocoria (inequality of pupillary size) implies disease of the efferent (motor) nerve, iris or muscles of the pupil.

Light-near dissociation

Here the light reflex is absent or sluggish but the near response is normal. The causes are shown in Table 18.1.

Argyll Robertson pupil

This is caused by neurosyphilis and is characterized by the following:

- Involvement is usually bilateral but asymmetrical.
- The pupils are small and irregular.
- Light-near dissociation.
- The pupils are very difficult to dilate.

Adie pupil

Adie (tonic) pupil is caused by denervation of the post-ganglionic supply to the sphincter pupillae and the ciliary muscle, which may follow a viral illness. It typically affects young adults and is unilateral in 80% of cases.

1. Signs
- Large and regular pupil.

Table 18.1 Causes of light-near dissociation

1. Uniiateral
- afferent conduction defect
- Adie pupil
- herpes zoster ophthalmicus
- aberrant regeneration of third nerve

2. Biiateral
- neurosyphilis
- type 1 diabetes
- myotonic dystrophy
- Parinaud dorsal midbrain syndrome
- familial amyloidosis
- encephalitis
- chronic alcoholism

- Light reflex is absent or sluggish and is associated with vermiform movements of the pupillary border, visible on the slit-lamp.
- The pupil responds slowly in the near reflex, following which redilatation is slow.
- Accommodation may manifest similar tonicity, in that once a near object has been fixated the time taken to refocus in the distance (relax the ciliary muscle) is prolonged.
- In long-standing cases the pupil may become small ('little old Adie').

2. **Associations**, in some cases, are diminished deep tendon reflexes (Holmes–Adie syndrome) and autonomic nerve dysfunction.
3. **Pharmacological testing.** If 2.5% mecholyl or 0.125% pilocarpine is instilled into both eyes, the normal pupil will not constrict, but the abnormal pupil will because of denervation hypersensitivity. Some diabetic patients may also show this response and very occasionally both pupils constrict in normal individuals.

Oculosympathetic palsy (Horner syndrome)

The causes of Horner syndrome are shown in Table 18.2.

Clinical features

- Mild ptosis (usually 1–2 mm) as a result of weakness of Müller muscle (Fig. 18.67).
- Slight elevation of the inferior eyelid as a result of weakness of the inferior tarsal muscle.
- Miosis resulting from the unopposed action of the sphincter pupillae, with resultant anisocoria which is accentuated in dim light, since the Horner pupil will not dilate, like its fellow.
- Normal reactions to light and near.

Table 18.2 Causes of Horner syndrome

1. **Central (first-order neurone)**
   - brain stem disease (tumours, vascular, demyelination)
   - syringomyelia
   - lateral medullary (Wallenberg) syndrome
   - spinal cord tumours
2. **Preganglionic (second-order neurone)**
   - Pancoast tumour
   - carotid and aortic aneurysms and dissection
   - neck lesions (glands, trauma, postsurgical)
3. **Postganglionic (third-order neurone)**
   - cluster headaches (migrainous neuralgia)
   - internal carotid artery dissection
   - nasopharyngeal tumours
   - otitis media
   - cavernous sinus mass

Fig. 18.67
Right Horner syndrome

- Reduced ipsilateral sweating, but only if the lesion is below the superior cervical ganglion because the fibres supplying the skin of the face run along the external carotid artery.
- Hypochromic heterochromia (irides of different colour—Horner is lighter) may be seen if the lesion is congenital or long-standing.
- The pupil is slow to dilate.
- Less important signs include hyperactive accommodation, ocular hypotony and conjunctival hyperaemia.

Pharmacological tests

Cocaine confirms the diagnosis. Hydroxyamphetamine (Paredrine) may be used to differentiate a preganglionic from a postganglionic lesion. Adrenaline may also be used to assess denervation supersensitivity.

1. **Cocaine 4%** is instilled into both eyes.
   - *Result*: the normal pupil will dilate but the Horner pupil will not.
   - *Rationale*: noradrenaline (NA) released at the postganglionic sympathetic nerve endings is reuptaken by the nerve endings, thus terminating its action. Cocaine blocks this uptake. NA therefore accumulates and causes pupillary dilatation. In Horner syndrome, there is no NA being secreted in the first place; therefore cocaine has no effect. Cocaine thus confirms the diagnosis of Horner sydrome.
2. **Hydroxyamphetamine 1%** is instilled into both eyes.
   - *Result*: in a preganglionic lesion both pupils will dilate (Fig. 18.68) whereas in a postganglionic lesion the Horner pupil will not. (This needs to be performed the following day, after the effects of cocaine have worn off.)
   - *Rationale*: hydroxyamphetamine potentiates the release of NA from postganglionic nerve endings. If this neurone is intact (a lesion of the first- or second-order neurone, and also the normal eye) NA will be released and the pupil will dilate. In a lesion of the third-order (postganglionic) neurone there can be no dilatation since the neurone is destroyed.
3. **Adrenaline 1:1000** is instilled into both eyes.
   - *Result*: in a preganglionic lesion neither pupil will dilate because adrenaline is rapidly destroyed by monoamine

Fig. 18.68
(a) Right preganglionic Horner syndrome; (b) bilateral mydriasis following instillation of hydroxyamphetamine into both eyes

oxidase: in a postganglionic lesion, the Horner pupil will dilate and ptosis may be temporarily relieved because adrenaline is not broken down due to the absence of monoamine oxidase.

- *Rationale*: a muscle deprived of its motor supply manifests heightened sensitivity to the excitatory neurotransmitter secreted by its motor nerve. In Horner syndrome the dilator pupillae muscle similarly manifests 'denervation hypersensitivity' to adrenergic neurotransmitters. Therefore adrenaline, even in minute concentrations, produces marked dilatation of the Horner pupil.

Nystagmus

Introduction

Physiological principles

Nystagmus is a repetitive, involuntary, to-and-fro oscillation of the eyes, which may be physiological or pathological. Thus nystagmus that occurs in response to rotation of an optokinetic drum or of the body in space is normal and acts to preserve clear vision. Ocular movements that bring about fixation on an object of interest are called foveating and those that move the fovea away from the object are defoveating. In pathological nystagmus, each cycle of movement is usually initiated by an involuntary defoveating drift of the eye away from the object of interest, followed by a returning refixational saccadic movement. The plane of nystagmus may be horizontal, vertical, torsional or non-specific. The amplitude of nystagmus refers to how far the eyes move, while the frequency refers to how often the eyes oscillate. On the basis of amplitude, nystagmus may be fine or coarse, while the frequency may be high, moderate or low.

Classification

1. **Jerk nystagmus** is saccadic with a slow defoveating 'drift' movement and a fast corrective refoveating saccadic movement. The direction of nystagmus is described in terms of the direction of the fast component, so that jerk nystagmus may be right, left, up, down or rotatory. Jerk nystagmus can be divided into gaze-evoked (i.e. vestibular) and gaze-paretic, which is slow and usually indicates brain stem damage.
2. **Pendular nystagmus** is non-saccadic in that both the foveating and defoveating movements are slow (i.e. the velocity of nystagmus is equal in both directions).
   - Congenital pendular nystagmus is horizontal, conjugate and tends to convert to jerk on lateral gaze.
   - Acquired pendular nystagmus has horizontal, vertical and torsional components.
   - If the horizontal and vertical components of pendular nystagmus are in phase (i.e. occur simultaneously) the perceived direction becomes oblique.
   - If the horizontal and vertical components are out of phase the direction becomes elliptic or rotatory.
3. **Mixed nystagmus** involves pendular nystagmus in the primary position and jerk nystagmus on lateral gaze.

The characteristics of any form of nystagmus can be documented using the scheme shown in Fig. 18.69.

Physiological nystagmus

1. **End-point nystagmus** is a fine jerk nystagmus of moderate frequency found when the eyes are in extreme positions of gaze. The fast phase is in the direction of gaze.
2. **Optokinetic nystagmus** is a jerk nystagmus induced by moving repetitive targets across the visual field. The slow phase is a pursuit movement in which the eyes follow the target; the fast phase is a saccadic movement in the opposite direction as the eyes fixate on the next target. If the optokinetic tape or drum is moved from right to left, the left parieto-occipital region controls the slow (pursuit) phase to the left, and the left frontal lobe controls the rapid (saccadic) phase to the right. Optokinetic nystagmus is useful for detecting malingerers who feign blindness and for testing visual acuity in the very young. It may also be helpful in determining the cause of an isolated homonymous hemianopia (*see* below).
3. **Vestibular nystagmus** is a jerk nystagmus caused by altered input from the vestibular nuclei to the horizontal gaze centres. The slow phase is initiated by the vestibular nuclei and the fast phase by the brain stem and fronto-mesencephalic pathway. Rotatory nystagmus is usually caused by pathological conditions affecting the vestibular system. Vestibular nystagmus may be elicited by caloric stimulation as follows:
   - When *cold* water is poured into the *right ear* the patient will develop *left* jerk nystagmus (i.e. fast phase to the left).

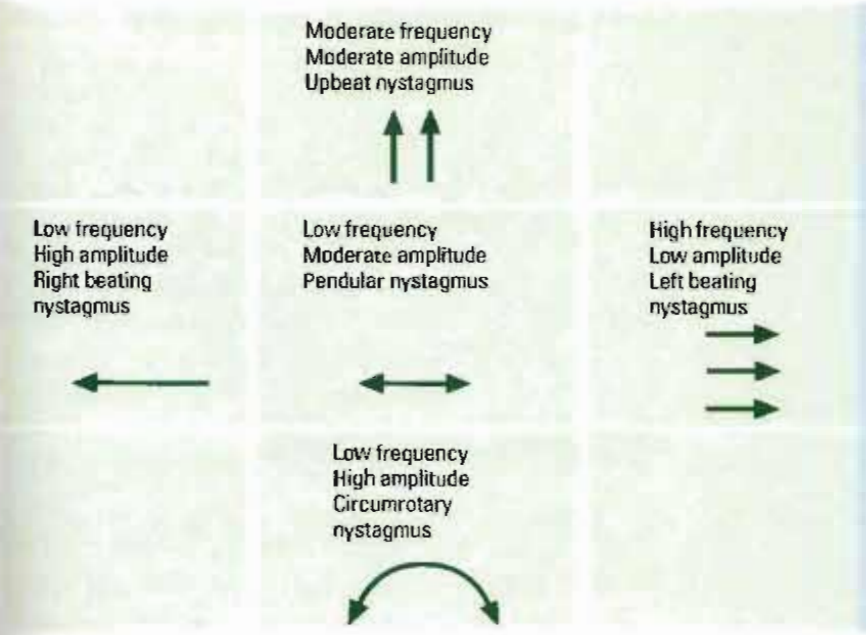


Fig. 18.69
Scheme for documenting nystagmus (Courtesy of J. Ferris)

- When *warm* water is poured into the *right ear* the patient will develop *right* jerk nystagmus (i.e. fast phase to the right). A useful mnemonic is 'COWS' (cold–opposite, warm–same) indicating the direction of the nystagmus.
- When cold water is poured into both ears simultaneously, a jerk nystagmus with the fast phase upwards develops: warm water in both ears elicits nystagmus with the fast phase downwards (cold 'slows things down').

Motor imbalance nystagmus

Motor imbalance nystagmus is the result of primary defects in the efferent mechanisms.

Congenital nystagmus

1. **Inheritance** may be XL recessive or AD.
2. **Presentation** is about 2–3 months after birth and persists throughout life.
3. **Signs**
   - Uniplanar horizontal nystagmus, usually of the jerk type.
   - It may be dampened by convergence and is not present during sleep.
   - There is usually a null point: a position of gaze in which nystagmus is minimal.
   - In order to move the eyes into the null point, an abnormal head posture may be adopted.

Spasmus nutans

1. **Presentation** of this rare condition is between 3 and 18 months.
2. **Signs**
   - Unilateral or bilateral, small-amplitude, high-frequency horizontal nystagmus associated with head nodding.
   - It is frequently asymmetrical with increased amplitude in abduction.
   - Vertical and torsional components may be present.
3. **Causes**
   - Idiopathic which spontaneously resolves by age 3 years.
   - Glioma of anterior visual pathway, empty sella syndrome and porencephalic cyst.

Latent nystagmus

This is associated with infantile esotropia and dissociated vertical deviation (*see* Chapter 16). It is characterized by the following:

- With both eyes open there is no nystagmus.
- Horizontal nystagmus, becomes apparent on covering one eye or reducing the amount of light reaching the eye.
- Fast phase is in the direction of the uncovered fixating eye.
- Occasionally, an element of latency may be superimposed on a manifest nystagmus so that when one eye is covered the amplitude of nystagmus increases (latent-manifest nystagmus).

Periodic alternating nystagmus

1. **Signs**
   - Conjugate horizontal jerk nystagmus that periodically reverses its direction.
   - Each cycle may be divided into active and quiescent phases as follows.
   - During the active phase, the amplitude, frequency and slow-phase velocity of nystagmus first progressively increase, then decrease.

- This is followed by a short, quiet interlude, lasting 4–20 seconds, during which time the eyes are steady and show low-intensity, often pendular movements.
- A similar sequence in the opposite direction occurs thereafter, the whole cycle lasting between 1 and 3 minutes.

2. **Causes** include cerebellar disease, demyelination, ataxia telangiectasia (Louis–Bar syndrome) and drugs such as phenytoin.

Convergence–retraction nystagmus

This is caused by co-contraction of the extraocular muscles, particularly the medial recti.

1. **Signs**
   - Jerk nystagmus is induced by passing an OKN tape downwards.
   - The upward refixation saccade brings the two eyes towards each other in a convergence movement.
   - Associated with retraction of the globe into the orbit.
2. **Causes** include lesions of the pretectal area such as pinealomas and vascular accidents.

Downbeat nystagmus

1. **Signs**. Vertical nystagmus with the fast phase beating downwards, which is more easily elicited in downgaze.
2. **Causes**
   - Lesions of the craniocervical junction at the foramen magnum such as an Arnold–Chiari malformation and syringobulbia.
   - Drugs such as lithium, phenytoin, carbamazepine and barbiturates.
   - Wernicke encephalopathy, demyelination and hydrocephalus.

Upbeat nystagmus

1. **Signs**. Vertical nystagmus with the fast phase beating upwards.
2. **Causes** include posterior fossa lesions, drugs and Wernicke encephalopathy.

See-saw nystagmus of Maddox

1. **Signs**. Pendular nystagmus, in which one eye elevates and intorts while the other depresses and extorts; the eyes then reverse direction.
2. **Causes** include parasellar tumours often producing bitemporal hemianopia, syringobulbia and brain stem stroke.

Ataxic nystagmus

This is a horizontal jerk nystagmus which occurs in the abducting eye of a patient with an internuclear ophthalmoplegia (*see* later).

Sensory deprivation nystagmus

Sensory deprivation (ocular) nystagmus is caused by defective vision. Horizontal and pendular, it can often be dampened by convergence. The severity depends on the degree of visual loss. An abnormal head posture may be adopted to decrease the amplitude of the nystagmus. It is caused by severe impairment of central vision in early life (e.g. congenital cataract, macular hypoplasia). In general, children who sustain bilateral loss of central vision before the age of 2 years develop nystagmus.

Nystagmoid movements

Nystagmoid movements resemble nystagmus but differ in that the initial, pathological defoveating movement is a saccadic intrusion.

Ocular flutter and opsoclonus

1. **Signs**
   - Saccadic oscillations with no intersaccadic interval.
   - In ocular flutter they are purely horizontal and in opsoclonus they are multiplanar.
2. **Causes** include viral encephalitis, myoclonic encephalopathy in infants ('dancing eyes and dancing feet'), transient (idiopathic) in healthy neonates and drug-induced (lithium, amitriptyline and phenytoin).

Ocular bobbing

1. **Signs**. Rapid, conjugate, downward eye movements with a slow drift up to the primary position.
2. **Causes** include pontine lesions (usually haemorrhage), cerebellar lesions compressing the pons and metabolic encephalopathy.

Supranuclear disorders of ocular motility

Conjugate eye movements

Conjugate eye movements or 'versions' are binocular movements in which the eyes move synchronously and symmetrically in the same direction. The three main types are: (a) *saccadic*, (b) *smooth pursuit* and (c) *non-optical reflex*. Saccadic and pursuit movements are controlled at both cerebral and brain stem levels. Supranuclear disturbances produce gaze palsies, characterized by absence of diplopia and normal vestibulo-ocular reflexes (e.g. oculocephalic movements and caloric stimulation).

Saccadic movements

1. **The function** of saccadic (fixating) movements is to place the object of interest on to the fovea rapidly or to move the eyes from one object to another. This can be done voluntarily or reflexly, triggered by the presence of an object in the peripheral visual field. Voluntary saccades are similar to the gunnery system of rapidly locating a moving target.
2. **The pathway** for horizontal saccades originates in the premotor cortex (the frontal eye fields). From there, fibres pass to the *contralateral* horizontal gaze centre in the pontine paramedian reticular formation (PPRF). Each frontal lobe therefore initiates contralateral saccades. Irritative lesions may therefore cause ocular deviation to the opposite side.

Smooth pursuit movements

1. **The function** of pursuit movements is to maintain fixation on a target once it has been located by the saccadic system. The stimulus is movement of the image near the fovea. The movements are slow and smooth.
2. **The pathway** originates in the peristriate cortex of the occipital lobe. The fibres descend and terminate in the *ipsilateral* horizontal gaze centre in the PPRF. Each occipital lobe therefore controls pursuit to the ipsilateral side.

Non-optical reflexes

1. **The function** of non-optical (vestibular) reflexes is to maintain eye position with respect to any changes of head and body position.
2. **The pathway** originates in the labyrinths and proprioceptors in the neck muscles which mediate information concerning head and neck movements. Afferent fibres synapse in the vestibular nuclei and pass to the horizontal gaze centre in the PPRF.

Horizontal gaze palsies

Applied anatomy

Horizontal eye movements are generated from the horizontal gaze centre in the PPRF (Fig. 18.70). From here fibres connect to the ipsilateral sixth nerve nucleus to abduct the ipsilateral eye. To adduct the contralateral eye, fibres from the PPRF also cross the midline at the level of the pons and pass up the contralateral medial longitudinal fasciculus (MLF) to the medial rectus subnucleus in the contralateral third nerve complex (which also receives independent descending input from the vergence control centres). Stimulation of the PPRF on one side therefore causes a conjugate movement of the eyes to the same side. It is important to remember that once the MLF leaves the PPRF, it crosses the midline immediately, and then ascends on the contralateral side. Loss of normal horizontal eye movements occurs when these pathways are disrupted. The causes are shown in Table 18.3.

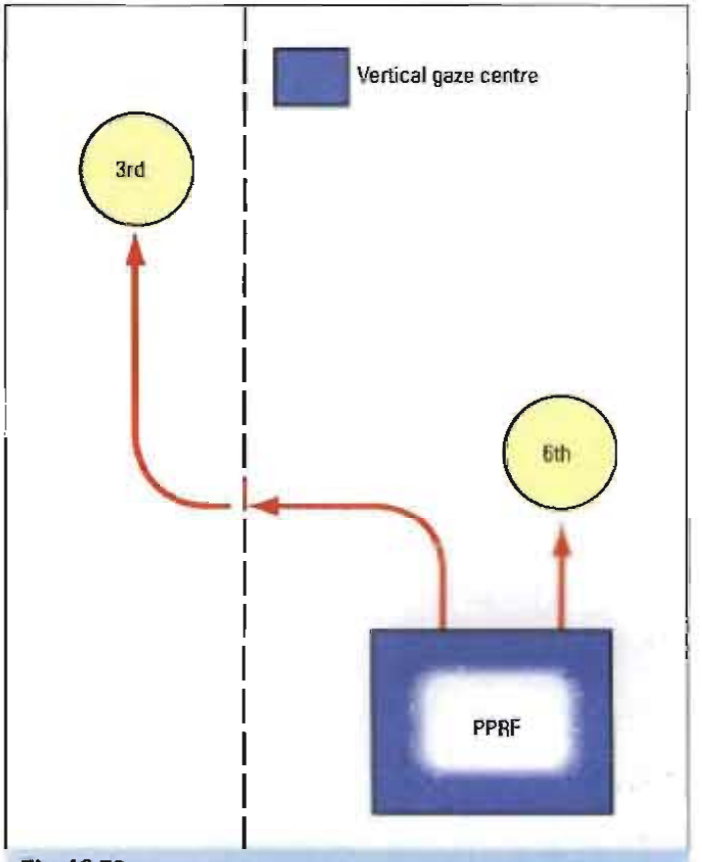


Fig. 18.70
Anatomical pathways for horizontal eye movements

Table 18.3 Causes of internuclear ophthalmoplegia

- demyelination
- vascular disease
- tumours of the brain stem and fourth ventricle
- trauma
- encephalitis
- hydrocephalus
- progressive supranuclear palsy
- drug-induced
- remote effects of carcinoma

Signs

1. **A PPRF** lesion gives rise to an ipsilateral horizontal gaze palsy (inability to look in the direction of the lesion).
2. **A MLF** lesion is responsible for the clinical syndrome of internuclear ophthalmoplegia (INO). A left internuclear ophthalmoplegia is characterized by the following:
   - On right gaze there is defective left adduction and ataxic nystagmus of the right eye (Fig. 18.71a).
   - Left gaze is normal (Fig. 18.71b).
   - Convergence is intact if the lesion is discrete.
   - Vertical nystagmus on attempted upgaze.

Fig. 18.71
Left internuclear ophthalmoplegia. (a) Defective left adduction on right gaze; (b) normal left gaze

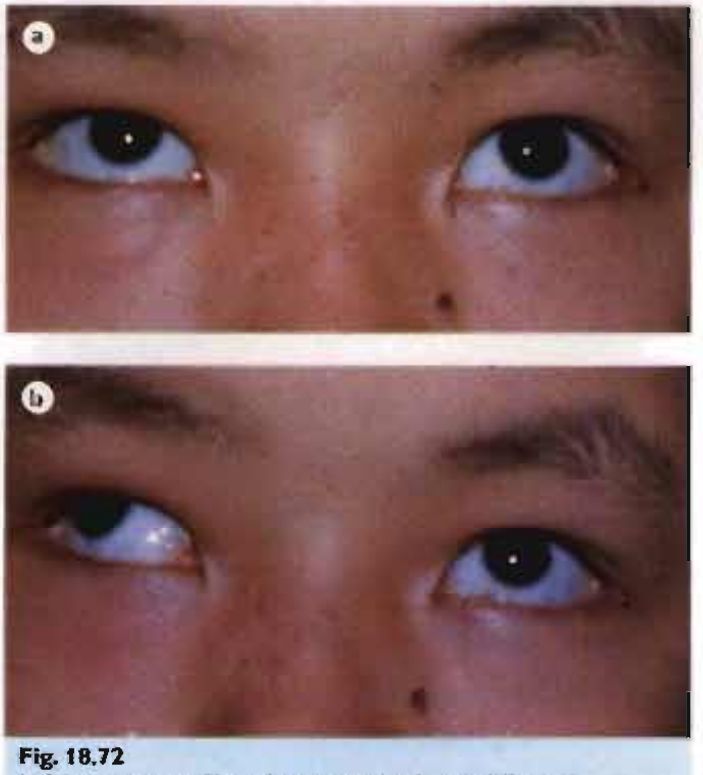


Fig. 18.72
Left 'one-and-a-half syndrome'. (a) Defective left gaze; (b) defective left adduction and normal right abduction on right gaze (Courtesy of K. Nischal)

3. **PPRF** and **MLF** combined lesions on the same side give rise to the 'one-and-a-half' syndrome'. A left lesion is characterized by:
   - Ipsilateral gaze palsy. Figure 18.72a shows the patient attempting left gaze.
   - Ipsilateral internuclear ophthalmoplegia. Figure 18.72b shows the patient attempting right gaze.
   - The only residual movement is abduction of the contralateral eye, which also exhibits ataxic nystagmus.

Vertical gaze palsies

Applied anatomy

Vertical eye movements are generated from the vertical gaze centre known as the rostral interstitial nucleus of the MLF, which lies in the midbrain just dorsal to the red nucleus. From the vertical gaze centre, impulses pass to the subnuclei of the eye muscles controlling vertical gaze in both eyes. Cells mediating upward and downward eye movements are intermingled in the vertical gaze centre, although selective paralysis of upgaze and downgaze may occur in spite of this.

Parinaud dorsal midbrain syndrome

1. **Signs**
   - Supranuclear upgaze palsy (Fig. 18.73a).
   - Straight eyes in the primary position (Fig. 18.73b)
   - Normal downgaze (Fig. 18.73c).
   - Large pupils with light-near dissociation.
   - Lid retraction (Collier sign).
   - Paralysis of convergence.
   - Convergence–retraction nystagmus.
2. **Causes**
   a. ***In children.*** Aqueduct stenosis, meningitis and pinealoma (Fig. 18.74).
   b. ***In young adults.*** Demyelination, trauma and arteriovenous malformations.
   c. ***In the elderly.*** Midbrain vascular accidents, mass lesions involving the periaqueductal grey matter and posterior fossa aneurysms.

Progressive supranuclear palsy

Progressive supranuclear palsy (Steele–Richardson–Olszewski syndrome) is a severe degenerative disease which presents in old age and is characterized by:

- Supranuclear gaze palsy, which initially primarily affects downgaze.
- As the disease progresses upgaze is also affected.
- Horizontal movements subsequently become impaired and eventually a global gaze palsy develops.
- Pseudobulbar palsy.
- Extrapyramidal rigidity, gait ataxia and dementia.

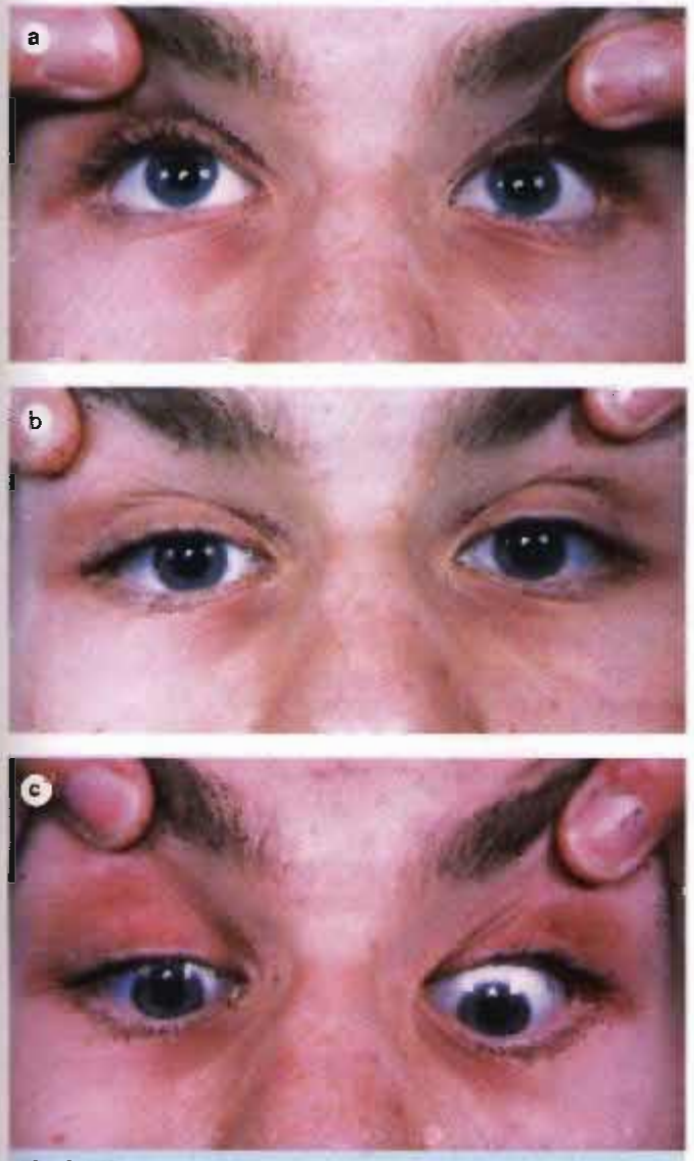


Fig. 18.73
Parinaud dorsal midbrain syndrome. (a) Defective upgaze; (b) straight eyes in primary position; (c) normal downgaze
(Courtesy of D. Thomas)

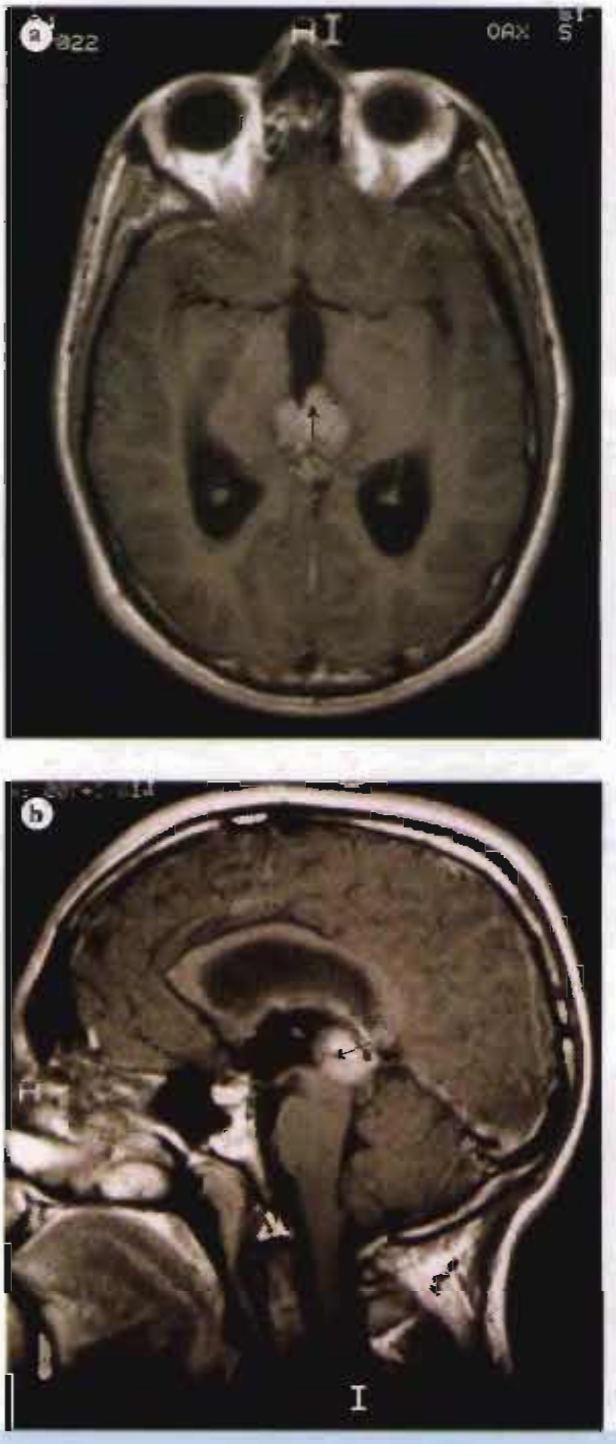


Fig. 18.74
T1-weighted MRI scan showing a pinealoma.
(a) axial view; (b) sagittal view—note dilated ventricles
(Courtesy of D. Thomas)

Third nerve

Applied anatomy

Nuclear complex

The nuclear complex of the third (oculomotor) nerve is situated in the midbrain at the level of the superior colliculus, ventral to the sylvian aqueduct (Fig. 18.75). It is composed of the following paired and unpaired subnuclei:

1. **Levator subnucleus** is an unpaired caudal midline structure which innervates both levator muscles. Lesions confined to this area will therefore give rise to bilateral ptosis.
2. **Superior rectus subnuclei** are paired; each innervates the respective contralateral superior rectus. A nuclear

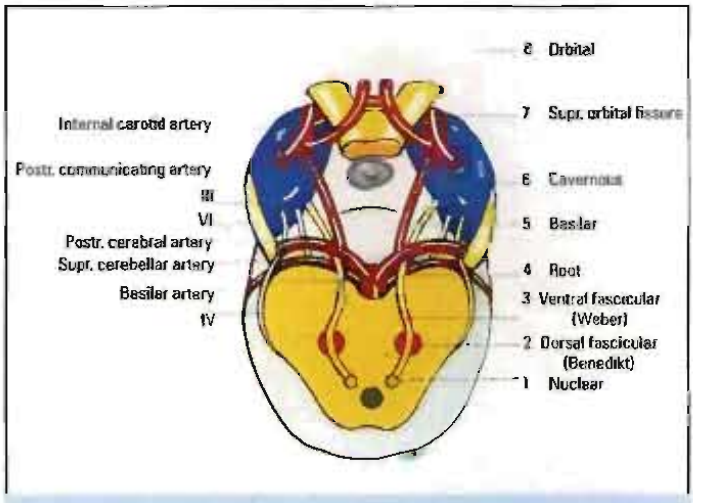


Fig. 18.75
Dorsal view of the course of the third nerve

third nerve palsy will spare the ipsilateral and affect the contralateral superior rectus.

3. **Medial rectus, inferior rectus** and **inferior oblique subnuclei** are paired and innervate their corresponding ipsilateral muscles. Lesions confined to the nuclear complex are relatively uncommon. The most frequent causes are vascular disease, primary tumours and metastases. Involvement of the paired medial rectus subnuclei causes a wall-eyed bilateral internuclear ophthalmoplegia (WEBINO), characterized by exotropia, and defective convergence and adduction. Lesions involving the entire nucleus are often associated with involvement of the adjacent and caudal fourth nerve nucleus.

Fasciculus

The fasciculus consists of efferent fibres which pass from the third nerve nucleus through the red nucleus and the medial aspect of the cerebral peduncle. They then emerge from the midbrain and pass into the interpeduncular space. The causes of nuclear and fascicular lesions are similar, except that demyelination may affect the fasciculus.

1. **Benedikt syndrome** involves the fasciculus as it passes through the red nucleus and is characterized by ipsilateral third nerve palsy and contralateral extrapyramidal signs such as hemitremor.
2. **Weber syndrome** involves the fasciculus as it passes through the cerebral peduncle and is characterized by an ipsilateral third nerve palsy and a contralateral hemiparesis.
3. **Nothnagel syndrome** involves the fasciculus and the superior cerebellar peduncle and is characterized by ipsilateral third nerve palsy and cerebellar ataxia. Important causes include vascular disease and tumours.
4. **Claude syndrome** is a combination of Benedikt and Nothnagel syndromes.

Basilar part

The basilar part starts as a series of 'rootlets' which leave the midbrain on the medial aspect of the cerebral peduncle, before coalescing to form the main trunk. The nerve then passes between the posterior cerebral and superior cerebellar arteries, running lateral to and parallel with the posterior communicating artery (Fig. 18.76). As the nerve traverses the base of the skull along its subarachnoid course unaccompanied by any other cranial nerve, isolated third nerve palsies are commonly basilar. The following are two important causes:

1. **Aneurysm** of the posterior communicating artery, at its junction with the internal carotid artery, (Fig. 18.77) typically presents as an acute, painful third nerve palsy with involvement of the pupil.
2. **Head trauma**, resulting in extradural or subdural haematoma, may cause a tentorial pressure cone with downward herniation of the temporal lobe. This compresses the third nerve as it passes over the tentorial edge, initially causing irritative miosis followed by mydriasis and a total third nerve palsy (Fig. 18.78).

Intracavernous part

The third nerve then enters the cavernous sinus by piercing the dura just lateral to the posterior clinoid process. Within the cavernous sinus, the third nerve runs in the lateral wall above the fourth nerve (Fig. 18.79). In the anterior part of the cavernous sinus, the nerve divides into superior and inferior branches which enter the orbit through the superior orbital fissure within the annulus of Zinn. The following are important causes of intracavernous third nerve palsies:

1. **Diabetes**, which may cause a vascular palsy, which usually spares the pupil.

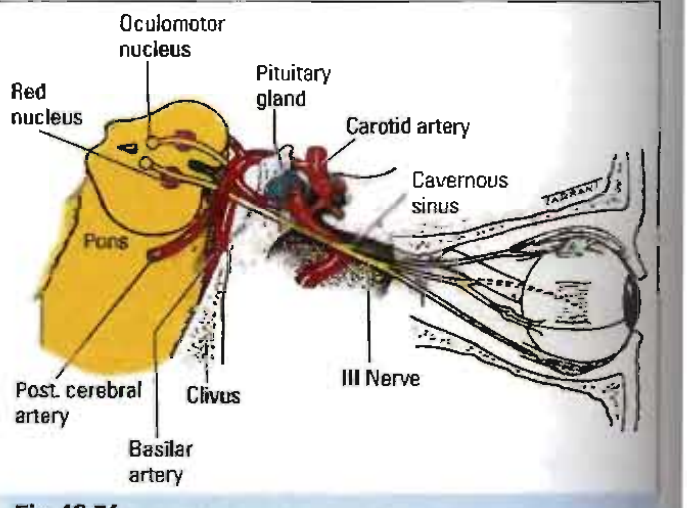


Fig. 18.76
Lateral view of the course of the third nerve

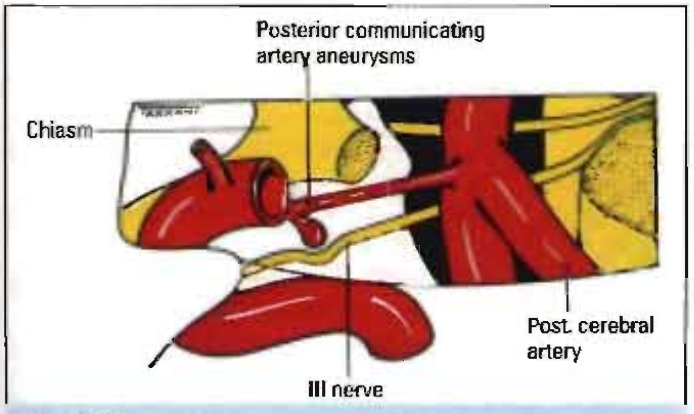


Fig. 18.77
Compression of the third nerve by a posterior communicating aneurysm

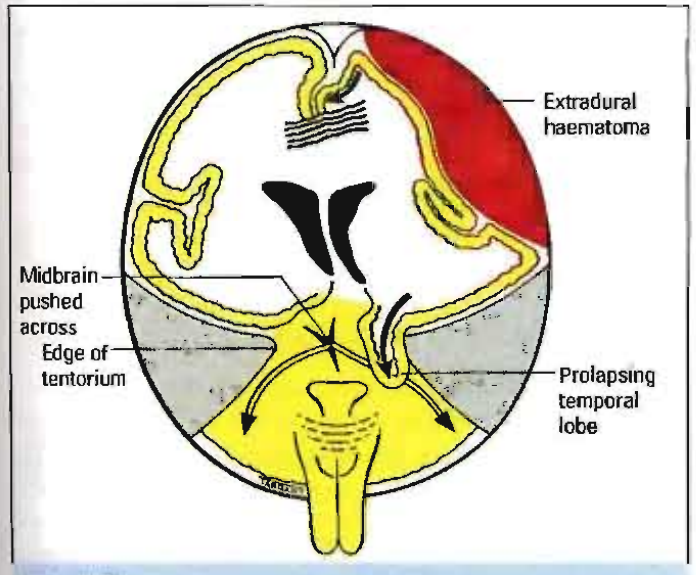


Fig. 18.78
Mechanism of third nerve palsy by extradural or subdural haematoma

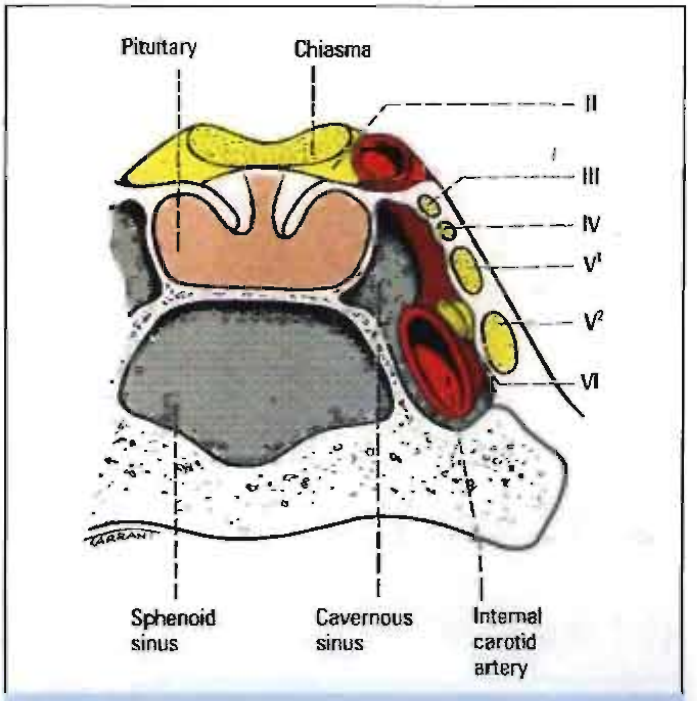


Fig. 18.79
Location of the cranial nerves in the cavernous sinus viewed from behind

2. **Pituitary apoplexy** (haemorrhagic infarction) may cause a third nerve palsy (e.g. after childbirth) if the gland swells laterally and impinges on the cavernous sinus.
3. **Intracavernous pathology** such as aneurysm, meningioma, carotid–cavernous fistula and granulomatous inflammation (Tolosa–Hunt syndrome) may all cause third nerve palsy. Because of its close proximity to other cranial nerves, intracavernous third nerve palsies are usually associated with involvement of the fourth and sixth nerves and the first division of the trigeminal nerve.

Intraorbital part

1. **Superior division** innervates the levator and superior rectus muscles.
2. **Inferior division** innervates the medial rectus, the inferior rectus and the inferior oblique muscles. The branch to the inferior oblique also contains preganglionic parasympathetic fibres from the Edinger–Westphal subnucleus, which innervate the sphincter pupillae and the ciliary muscle. Lesions of the inferior division are characterized by limited adduction and depression, and a dilated pupil. Both superior and inferior division palsies are commonly traumatic or vascular.

Pupillomotor fibres

Between the brain stem and the cavernous sinus, the pupillomotor parasympathetic fibres are located superficially in the superomedial part of the third nerve (Fig. 18.80). They derive their blood supply from the pial blood vessels, whereas the main trunk of the third nerve is supplied by the vasa nervorum. Involvement or otherwise of the pupil is of great importance because it frequently differentiates a 'surgical' from a 'medical' lesion. Pupillary involvement, like other features of third nerve palsy, may be complete or partial, and may demonstrate features of recovery. Mild mydriasis and non-reactivity may therefore be clinically significant.

1. **Surgical lesions** such as aneurysms, trauma and uncal herniation characteristically involve the pupil by compressing the pial blood vessels and the superficially located pupillary fibres.
2. **Medical lesions** such as hypertension and diabetes usually spare the pupil. This is because the microangiopathy associated with medical lesions involves the vasa nervorum, causing ischaemia of the main trunk of the nerve, sparing the superficial pupillary fibres.

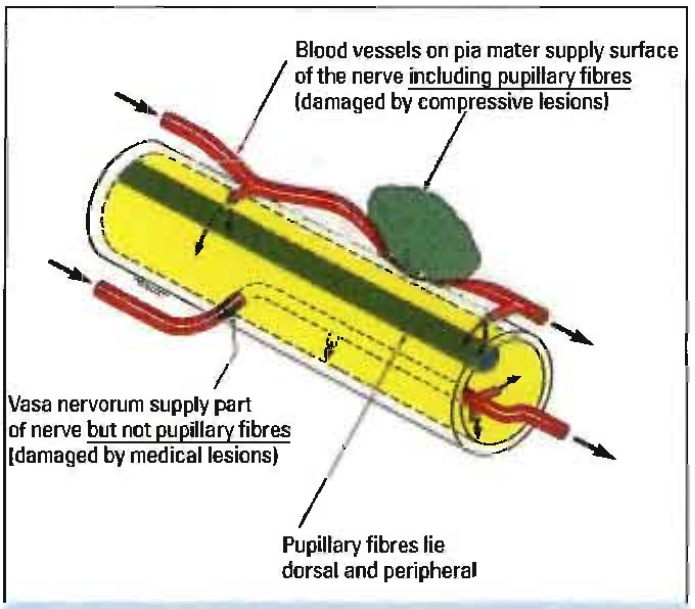


Fig. 18.80
Location of the pupillomotor fibres within the trunk of the third nerve

NB: These principles are, however, not infallible; pupil involvement may be seen in some diabetic-associated third nerve palsies, while pupillary sparing does not invariably exclude an aneurysm or some other compressive lesion. Sometimes pupillary involvement may be the only sign of a third nerve palsy (basal meningitis, uncal herniation).

Clinical aspects

Clinical features

1. **Signs** of a left third nerve palsy (Fig. 18.81).
   - Weakness of the levator causing profound ptosis, due to which there is often no diplopia (Fig. 18.81a).
   - Unopposed action of lateral rectus causing the eye to be abducted in the primary position (Fig. 18.81b).
   - The intact superior oblique muscle causes intorsion of the eye at rest, which increases on attempted downgaze.
   - Normal abduction because the lateral rectus is intact (Fig. 18.81c).
   - Weakness of medial rectus limiting adduction (Fig. 18.81d).
   - Weakness of superior rectus and inferior oblique, limiting elevation (Fig. 18.81e).
   - Weakness of inferior rectus limiting depression (Fig. 18.81f).
   - Parasympathetic palsy causing a dilated pupil associated with defective accommodation.
2. **Aberrant regeneration** may follow acute traumatic and aneurysmal, but not vascular, third nerve palsies. This is because the endoneural nerve sheaths, which may be breached in traumatic and compressive lesions, remain intact in vascular pathology. Bizarre defects in ocular motility (*see* Fig. 1.123), such as elevation of the upper eyelid on attempted adduction or depression (the pseudo-Graefe phenomenon), are caused by misdirection of regenerating axons which reinnervate the wrong extraocular muscle. The pupil may also be involved.

Causes of isolated third nerve palsy

1. **Idiopathic**: about 25% have no known cause.
2. **Vascular disease**, such as due to hypertension and diabetes, is the most common cause of a pupil-sparing third nerve palsy. All patients should therefore have blood pressure measurement, urinalysis and plasma glucose estimation. In most cases spontaneous recovery occurs within 3 months. Diabetic third nerve palsy is often associated with periorbital pain and may occasionally be the presenting feature of diabetes. The presence of pain is therefore not helpful in differentiating aneurysmal and diabetic third nerve palsy.

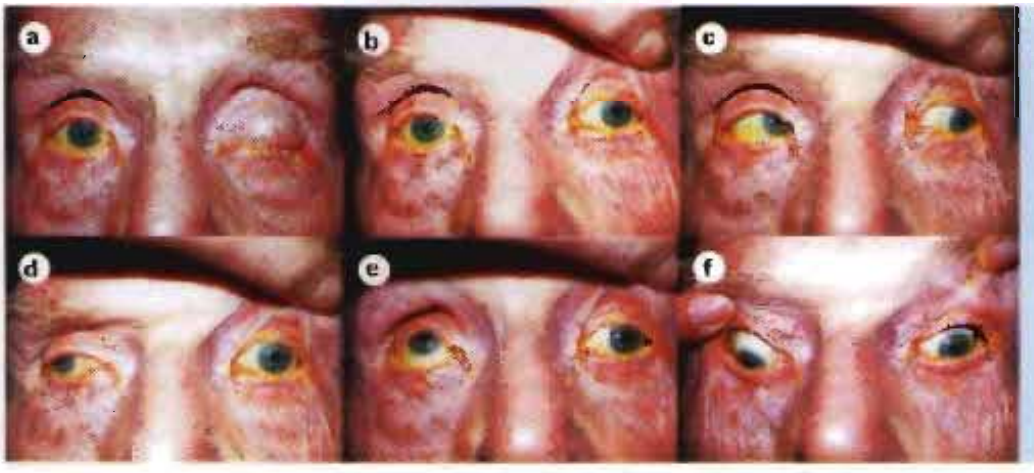


Fig. 18.81
Left third nerve palsy (*see text*)

3. **Trauma**, both direct and secondary to subdural haematoma with uncal herniation, is also a common cause. However, the development of third nerve palsy following relatively trivial head trauma, not associated with loss of consciousness, should alert the clinician to the possibility of an associated basal intracranial tumour which has caused the nerve trunk to be stretched and tethered.
4. **Aneurysm** of the posterior communicating artery at its junction with the internal carotid is a very important cause of an isolated painful third nerve palsy with involvement of the pupil.
5. **Miscellaneous** uncommon causes include tumours, syphilis and vasculitis associated with collagen vascular disorders.

Management

1. **Non-surgical** treatment options include the use of Fresnel prisms if the angle of deviation is small, uniocular occlusion to avoid diplopia (if ptosis is partial or recovering) and botulinum toxin injection into the uninvolved lateral rectus muscle to prevent its contracture before the deviation improves or stabilizes (*see* Chapter 16).
2. **Surgical** treatment, as with other ocular motor nerve palsies, should be contemplated only after all spontaneous improvement has ceased. This is usually not earlier than 6 months from the date of onset (*see* Chapter 16).

Fourth nerve

Applied anatomy

1. **Important features** of the fourth (trochlear) nerve are the following:
   - It is the only cranial nerve to emerge from the dorsal aspect of the brain.
   - It is a crossed cranial nerve; this means that the fourth nerve nucleus innervates the contralateral superior oblique muscle.
   - It is a very long and slender nerve.
2. **The nucleus** of the fourth nerve is located at the level of the inferior colliculi ventral to the sylvian aqueduct (Fig. 18.82). It is caudal to, and continuous with, the third nerve nuclear complex.
3. **The fasciculus** consists of axons which curve posteriorly around the aqueduct and decussate completely in the anterior medullary velum.
4. **The trunk** leaves the brain stem on the dorsal surface, just caudal to the inferior colliculus. It then curves laterally around the brain stem, runs forwards beneath the free edge of the tentorium, and (like the third nerve) passes between the posterior cerebral artery and the superior cerebellar artery. It then pierces the dura and enters the cavernous sinus.

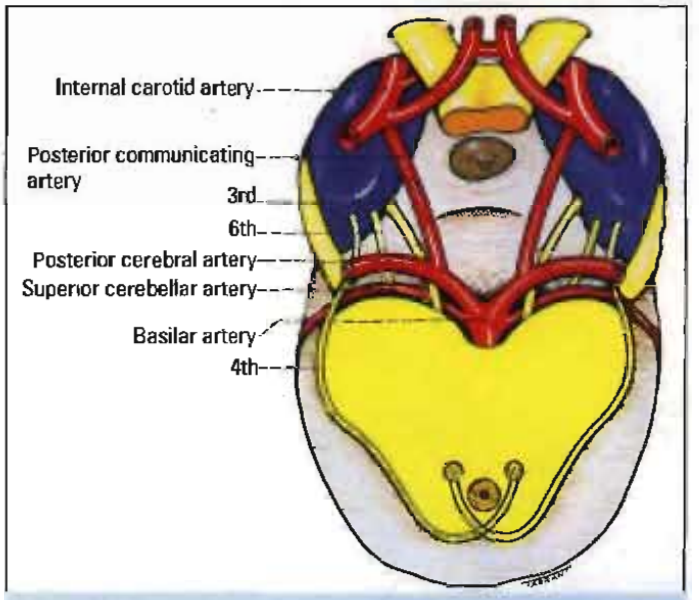


Fig. 18.82
Dorsal view of the course of the fourth nerve

5. **The intracavernous part** runs in the lateral wall of the sinus, inferiorly to the third nerve and above the first division of the fifth. In the anterior part of the cavernous sinus it rises and passes through the superior orbital fissure above and lateral to the annulus of Zinn.
6. **The intraorbital part** innervates the superior oblique muscle.

Clinical features

Acute onset of vertical diplopia in the absence of ptosis, combined with a characteristic head posture, strongly suggests fourth nerve disease. The features of nuclear, fascicular and peripheral fourth nerve palsies are clinically identical, except that nuclear palsies produce contralateral superior oblique weakness. A left fourth nerve palsy is illustrated.

1. **Signs**
   - Left limitation of depression in adduction due to superior oblique weakness (Fig. 18.83).

Fig. 18.83
Left fourth nerve palsy (see *text*)

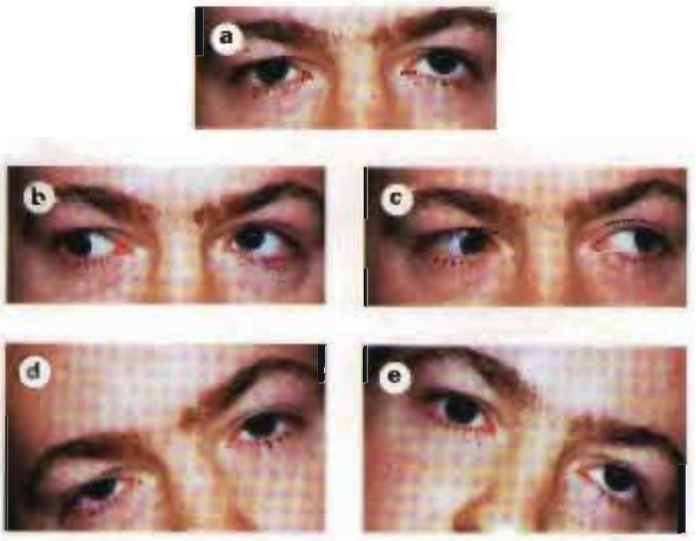


Fig. 18.84
Parks three step test. (a) Step 1; (b and c) step 2; (d and e) step 3 (see *text*)

- Excyclotorsion.
- Diplopia which is vertical, torsional and worse on looking down.
- Left hyperdeviation ('left over right') in the primary position when the uninvolved right eye is fixating due to weakness of the left superior oblique (Fig. 18.84a).
- The left hypertropia increases on right gaze (Fig. 18.84b) due to left inferior oblique overaction, and is minimal or absent in left gaze (Fig. 18.84c).

2. **Abnormal head posture** is adopted to avoid diplopia.
   - To intort the eye (alleviate excyclotorsion) there is contralateral head tilt.
   - To alleviate the inability to depress the eye in adduction, the face is turned to the right and the chin is depressed (*see* Fig. 16.16).

> *NB*: The left eye cannot look down and to the right, or intort; the head therefore does this and thus compensates.

3. **Bilateral** involvement is common and is characterized by:
   - Right hypertropia in left gaze, left hypertropia in right gaze.
   - Greater than 10° cyclodeviation on double Maddox rod test (*see* below).
   - V pattern esotropia.
   - Bilaterally positive Bielschowsky test (*see* below).

Special tests

1. **Parks three step test** is very useful in the diagnosis of fourth nerve palsy and is performed as follows:
   a. Step one. Assess which eye is hypertropic in the primary position. Left hypertropia (*see* Fig. 18.84a) may be caused by weakness of one of the following four muscles: the depressors of the left eye (superior oblique or inferior rectus) or the elevators of the right eye (superior rectus or inferior oblique).
   b. Step two. Determine whether the left hypertropia is greater in right gaze or left gaze (*see* Fig. 18.84b and c). Increase on left gaze implicates either the left inferior rectus or right inferior oblique. Increase on right gaze implicates either the left superior oblique or right superior rectus.
   c. Step three. The Bielschowsky head tilt test isolates the paretic muscle. With the patient fixating a straight ahead target at 3 metres, the head is manually tilted to the right and then to the left. Increase of left hypertropia on left head tilt (*see* Fig. 18.84e) implicates the left superior oblique and increase of left hypertropia on right head tilt implicates the left inferior rectus.
2. **Double Maddox rod test**
   - Red and green Maddox rods, with the cylinders vertical, are placed one in front of either eye.
   - Each eye will therefore perceive a more or less horizontal line of light.
   - In the presence of cyclodeviation, the line perceived by the paretic eye will be tilted and therefore distinct from that of the other eye.
   - One Maddox rod is then rotated until fusion (superimposition) of the lines is achieved.
   - The amount of rotation can be measured in degrees and indicates the extent of cyclodeviation.
   - A unilateral fourth nerve palsy is characterized by less than 10° of cyclodeviation.

Causes of isolated fourth nerve palsy

1. **Congenital** lesions are frequent, although symptoms may not develop until adult life. Examination of old photographs for the presence of an abnormal head posture may be helpful as is the presence of an increased vertical prism fusional range.
2. **Trauma** frequently causes bilateral fourth nerve palsy. The long and slender nerves are vulnerable as they decussate in the anterior medullary velum through impact with the tentorial edge.
3. **Vascular** lesions are common but aneurysms and tumours are rare.

Sixth nerve

Applied anatomy

Nucleus

The nucleus of the sixth (abducens) nerve lies at the mid level of the pons, ventral to the floor of the fourth ventricle, where it is closely related to the horizontal gaze centre. The fasciculus of the seventh nerve curves around the abducent nucleus and produces an elevation in the floor of the fourth ventricle (facial

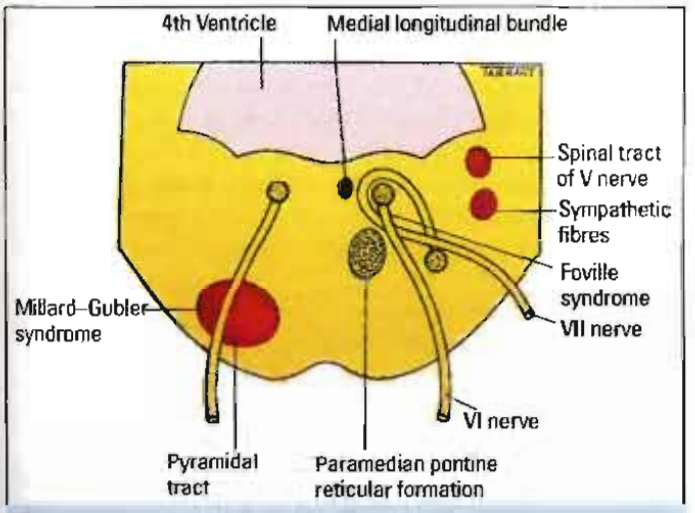


Fig. 18.85
The pons at the level of the sixth nerve nucleus

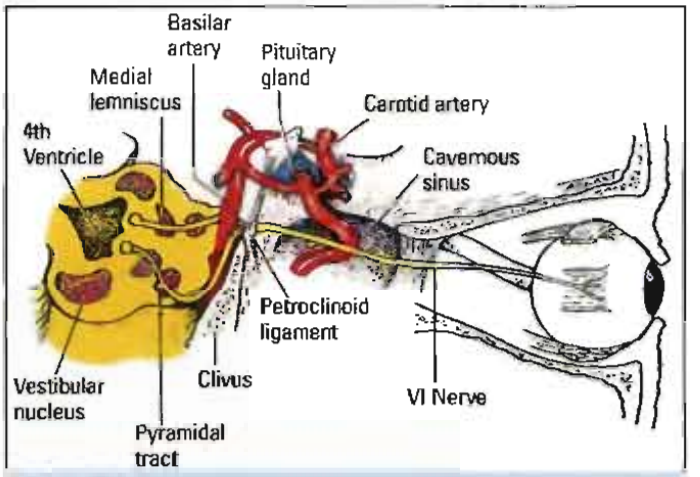


Fig. 18.86
Lateral view of the course of the sixth nerve

colliculus) (Fig. 18.85). An isolated sixth nerve palsy is therefore never nuclear in origin. A lesion in and around the sixth nerve nucleus causes the following signs:

- Ipsilateral weakness of abduction as a result of involvement of the sixth nerve.
- Failure of horizontal gaze towards the side of the lesion resulting from involvement of the horizontal gaze centre in the PPRF.
- Ipsilateral lower motor neurone facial nerve palsy caused by concomitant involvement of the facial fasciculus is also common.

Fasciculus

The fasciculus passes ventrally to leave the brain stem at the pontomedullary junction, just lateral to the pyramidal prominence.

1. **Foville syndrome** involves the fasciculus as it passes through the PPRF and is most frequently caused by vascular disease or tumours involving the dorsal pons. It is characterized by ipsilateral involvement of the fifth to eighth cranial nerves and central sympathetic fibres.
   - Fifth nerve: facial analgesia.
   - Sixth nerve palsy combined with a gaze palsy (PPRF).
   - Seventh nerve (nuclear or fascicular damage): facial weakness.
   - Eighth nerve: deafness.
   - Central Horner syndrome.
2. **Millard–Gubler** syndrome involves the fasciculus as it passes through the pyramidal tract and is most frequently caused by vascular disease, tumours or demyelination. It is characterized by the following:
   - Ipsilateral sixth nerve palsy.
   - Contralateral hemiplegia (since the pyramidal tracts decussate further inferiorly, in the medulla, to control contralateral voluntary movement).
   - Variable number of signs of a dorsal pontine lesion.

Basilar part

The basilar part leaves the brain stem at the pontomedullary junction and enters the prepontine basilar cistern. It then passes upwards close to the base of the skull and is crossed by the anterior inferior cerebellar artery (Fig. 18.86). It pierces the dura below the posterior clinoids and angles forwards over the tip of the petrous bone, passing through or around the inferior petrosal sinus, through Dorello canal (under the petroclinoid ligament), to enter the cavernous sinus. The following are important causes of damage to the basilar part of the nerve:

1. **Acoustic neuroma** may damage the sixth nerve at the pontomedullary junction (Fig. 18.87). It should be

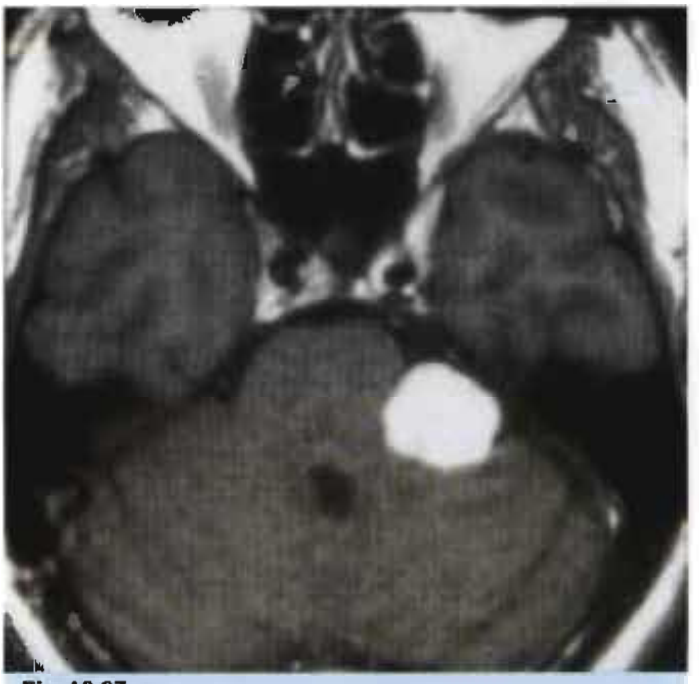


Fig. 18.87
Axial T1-weighted MRI scan with gadolinium showing an acoustic neuroma

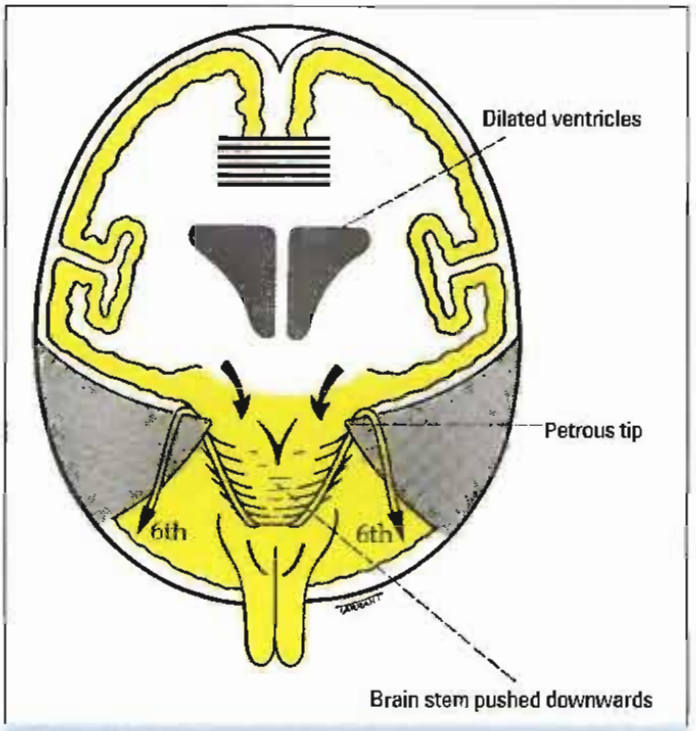


Fig. 18.88
Mechanism of bilateral sixth nerve palsies from raised intracranial pressure

emphasized that the first symptom of an acoustic neuroma is hearing loss and the first sign diminished corneal sensitivity. It is therefore very important to test hearing and corneal sensation in all patients with sixth nerve palsy.

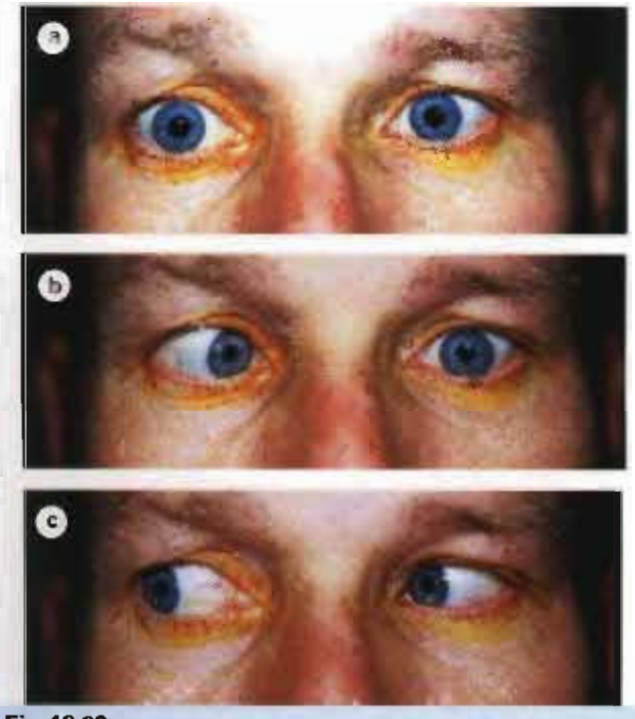


Fig. 18.89
Left sixth nerve palsy (see *text*)

2. **Nasopharyngeal tumours** may invade the skull and its foramina and damage the nerve during its basilar course.
3. **Raised intracranial pressure** caused by posterior fossa tumours or idiopathic intracranial hypertension may cause a downward displacement of the brain stem. This may stretch the sixth nerve over the petrous tip (Fig. 18.88) between its point of emergence from the brain stem and its point of entry into the cavernous sinus.

> ***NB:*** In this situation, sixth nerve palsy, which may be bilateral, is a false localizing sign.

4. **Basal skull fracture** may cause both unilateral and bilateral palsies.
5. **Gradenigo syndrome**, most frequently caused by mastoiditis or acute petrositis, may result in damage of the sixth nerve at the petrous tip. The latter is frequently accompanied by facial weakness and pain, and hearing difficulties.

Intracavernous and intraorbital parts

1. **The intracavernous part** runs forwards below the third and fourth nerves, as well as the first division of the fifth. Although the other nerves are protected within the wall of the sinus, the sixth is most medially situated and runs through the middle of the sinus in close relation to the internal carotid artery. It is therefore more prone to damage than the other nerves. Occasionally, an intracavernous sixth nerve palsy is accompanied by a postganglionic Horner syndrome (Parkinson sign) because in its intracavernous course the sixth nerve is joined by sympathetic branches from the paracarotid plexus. The causes of intracavernous sixth nerve and third nerve lesions are similar.
2. **The intraorbital part** enters the orbit through the superior orbital fissure within the annulus of Zinn to innervate the lateral rectus muscle.

Clinical aspects

Clinical features

1. **Signs** of a left sixth nerve palsy.
   - Left esotropia in the primary position due to unopposed action of the left medial rectus (Fig. 18.89a).
   - Marked limitation of left abduction due to weakness of the left lateral rectus (Fig. 18.89b).
   - Normal left adduction (Fig. 18.89c).
2. **Compensatory** face turn into the field of action of the paralysed muscle (i.e. to the left) to minimize diplopia, so that the eyes do not need to look towards the field of action of the paralysed muscle.
3. **Causes** of isolated sixth nerve palsies have already been mentioned.

> ***NB:*** Aneurysms rarely affect the sixth nerve but vascular causes are common.

Differential diagnosis

The following conditions may mimic sixth nerve palsy:

1. **Myasthenia gravis** can mimic virtually any ocular motility defect. Distinguishing features include variability of diplopia and other signs such as lid fatigue and Cogan twitch sign (*see* later).
2. **Restrictive thyroid myopathy** involving the medial rectus may give rise to limitation of abduction. Associated features include orbital and eyelid signs and a positive forced duction test (*see* Chapter 17).
3. **Medial orbital wall blowout fracture** with entrapment of the medial rectus giving rise to limitation of abduction (*see* Chapter 19).
4. **Orbital myositis** involving the lateral rectus is characterized by weakness of abduction and pain when this is attempted (*see* Chapter 17).
5. **Duane syndrome** is a congenital condition characterized by defective abduction and narrowing of the palpebral fissure on adduction (*see* Chapter 16).
6. **Convergence spasm** typically affects young adults and is characterized by convergence with miosis and increased accommodation.
7. **Divergence paralysis** is a rare condition which may be difficult to distinguish from unilateral or bilateral sixth nerve palsy. However, unlike sixth nerve palsy the esotropia may remain the same or diminish on lateral gaze.
8. **Infantile esotropia**

Chiasm

Applied anatomy

Pituitary gland

The sella turcica (Turkish saddle) is a deep saddle-shaped depression in the superior surface of the body of the sphenoid bone in which the pituitary gland lies (Fig. 18.90). The roof of the sella is formed by a fold of dura mater which stretches from the anterior to the posterior clinoids (diaphragma sellae). The optic nerves and chiasm lie above the diaphragma sellae; a visual field defect in a patient with a pituitary tumour therefore indicates suprasellar extension. Tumours less than 10 mm in diameter (microadenomas) often remain intrasellar, whereas those larger than 10 mm (macroadenomas) tend to manifest extrasellar extension. Posteriorly the chiasm is continuous with the optic tracts and forms the anterior wall of the third ventricle.

Chiasmal nerve pathways

Optic nerve fibres passing through the chiasm are arranged as follows:

1. **Lower nasal fibres** traverse the chiasm low and anteriorly. They are therefore most vulnerable to damage from expanding pituitary lesions, so the upper temporal quadrants of the visual fields are involved first.

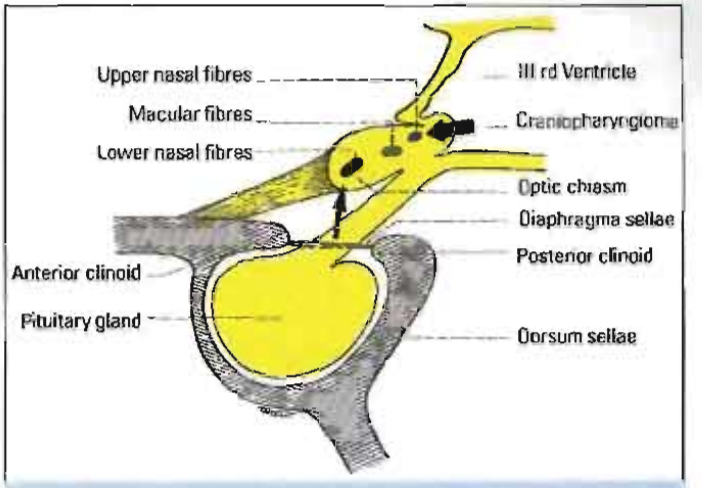


Fig. 18.90
Anatomy of the optic chiasm in relation to the pituitary gland

NB: The inferonasal fibres loop forwards into the contralateral optic nerve, before passing posteriorly into the optic tract (anterior knee of Wilbrand) and may therefore be affected by lesions affecting the posterior part of the optic nerve.

2. **Upper nasal fibres** traverse the chiasm high and posteriorly and therefore are involved first by lesions coming from above the chiasm (e.g. craniopharyngiomas). If the lower temporal quadrants of the visual field are affected more than the upper, a pituitary adenoma is unlikely.
3. **Macular fibres** decussate throughout the chiasm.

Anatomical variants

The following anatomical variations in the location of the chiasm may have important clinical significance (Fig. 18.91):

1. **Central chiasm**, which is present in about 80% of normals, lies directly above the sella so that expanding pituitary tumours will involve the chiasm first.
2. **Prefixed chiasm**, which is present in about 10% of normals, is located more anteriorly, over the tuberculum sellae, so that pituitary tumours involve the optic tracts first.
3. **Postfixed chiasm**, which is present in the remaining 10% of normals, is located more posteriorly, over the dorsum sellae, so that pituitary tumours are apt to damage the optic nerves first.

Parachiasmal vascular structures

1. **The cavernous sinuses** lie lateral to the sella so that laterally expanding pituitary tumours affect the cavernous sinus and may damage the intracavernous parts of the

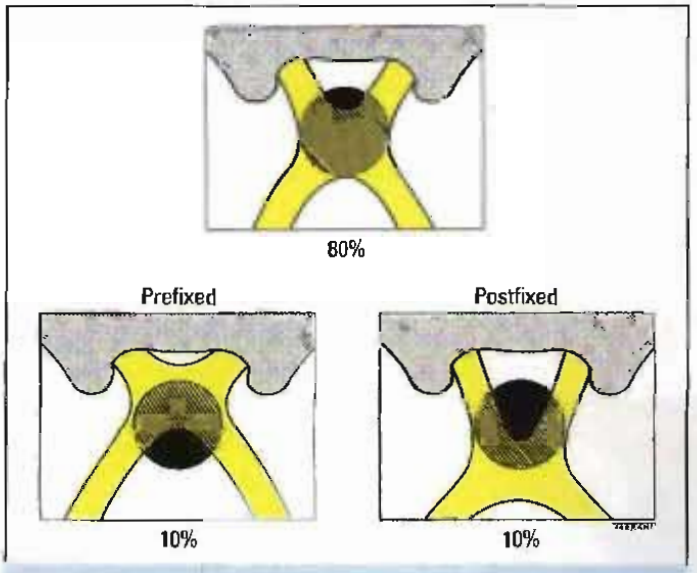


Fig. 18.91
Anatomical variations in position of the optic chiasm

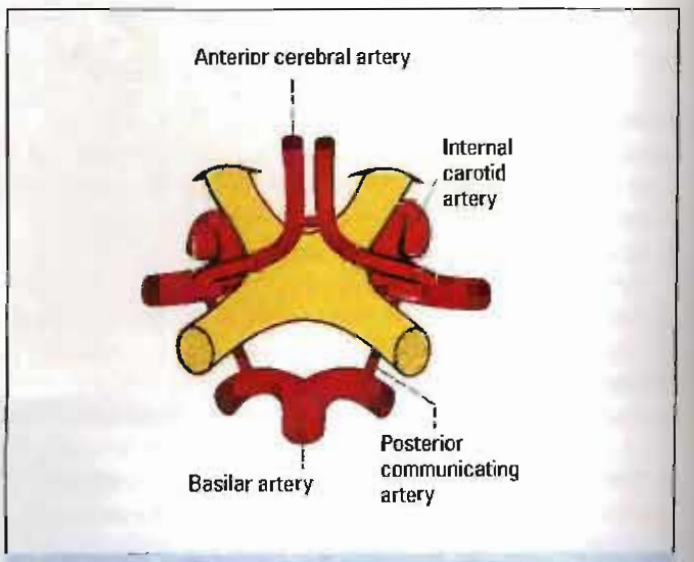


Fig. 18.92
Relationship between the chiasm and adjacent arteries

third, fourth and sixth cranial nerves. Conversely, aneurysms arising from the intracavernous part of the internal carotid artery may erode into the sella and mimic pituitary tumours.

2. **The internal carotid arteries** curve posteriorly and upwards from the cavernous sinus and lie immediately below the optic nerves (Fig. 18.92). They then ascend vertically alongside the lateral aspect of the chiasm. The precommunicating portion of the anterior cerebral artery is closely related to the superior surface of the chiasm and optic nerves. An aneurysm in this region can therefore compress the optic nerve (Fig. 18.93) or the chiasm.

Applied physiology

Pituitary hormones

The lobules of the anterior part of the pituitary gland are composed of six cell types. Five of these secrete hormones and the sixth (follicular cell) has no secretory function. The hormones secreted by the anterior pituitary gland are growth hormone (GH), prolactin, follicle-stimulating hormone (FSH), adrenocorticotrophic hormone (ACTH), thyroid-stimulating hormone (TSH), leutenizing hormone (LH) and beta-lipotrophin. Although pituitary adenomas are classified as basophil, acidophil and chromophobe, tumours of mixed-cell types are common and any of the six cell types may proliferate to produce an adenoma. The anterior pituitary is itself under the control of the various inhibiting and releasing factors which are synthesized in the hypothalamus and which pass to the anterior pituitary through the hypothalamo-hypophyseal portal system.

Causes of pituitary dysfunction

1. **Hyperpituitarism** (Fig. 18.94)
   - *a. **Basophil tumours*** secrete ACTH and cause Cushing disease (*see* Chapter 20).
   - *b. **Acidophil tumours*** secrete growth hormone, which causes gigantism in children and acromegaly in adults (*see* Chapter 20).
   - *c. **Chromophobe adenomas*** may secrete prolactin and are referred to as prolactinomas. Excessive levels of prolactin in women lead to the infertility–amenorrhoea–galactorrhoea syndrome, and in men cause hypogonadism, impotence, sterility, decreased libido and occasionally gynaecomastia and even galactorrhoea. Some chromophobe adenomas are non-secreting.
2. **Hypopituitarism**
   - *a. **Direct pressure*** on the secreting cells in the anterior pituitary by a mass. Secondary deposits are common in the pituitary but do not normally affect hormone secretion.
   - *b. **Vascular damage*** to the pituitary (e.g. pituitary apoplexy after childbirth—Sheehan syndrome).
   - *c. **Iatrogenic*** causes such as pituitary surgery and/or radiotherapy.
   - *d. **Interference*** with the synthesis of Inhibiting and releasing factors in the hypothalamus by gliomas or impediment of their transport in the portal system.

NB: The clinical features are dictated by both the pattern of hormone deficiency and the stage of growth and development of the patient at the time. Usually gonadotrophin secretion is impaired first, followed by that of growth hormone; deficiencies in other hormones occur later.

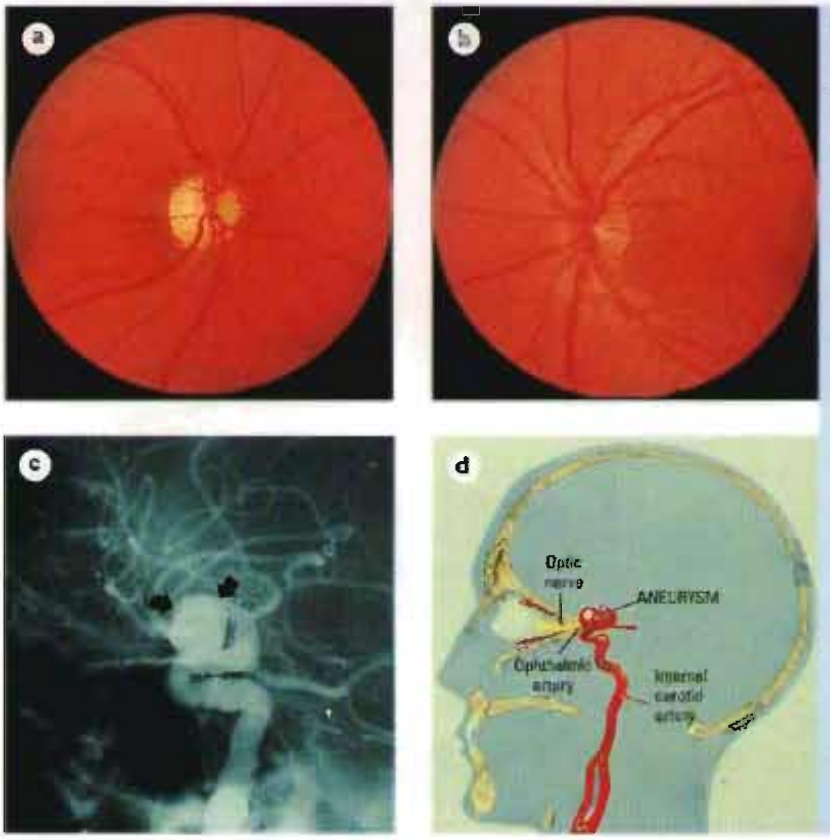


Fig. 18.93
Aneurysmal compression of the right optic nerve. (a) Right optic atrophy; (b) normal left disc; (c) angiogram showing the aneurysm (arrows); (d) schematic diagram (Courtesy of Wilmer Institute)

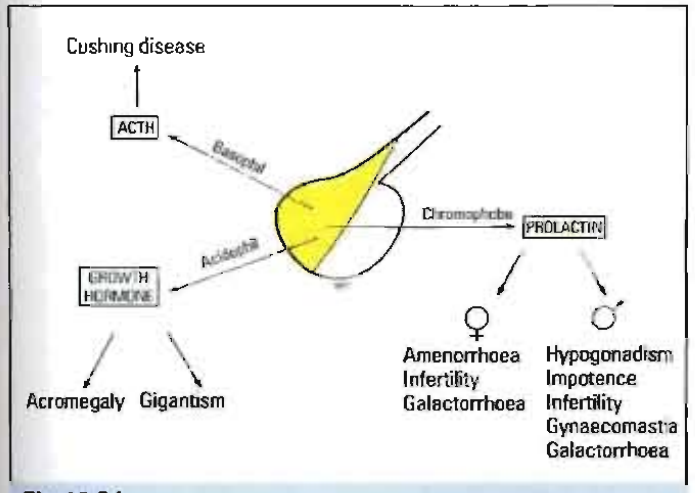


Fig. 18.94
Hormones secreted by anterior pituitary tumours

Causes of chiasmal disease

1. **Tumours** such as pituitary adenomas, craniopharyngiomas, meningiomas, gliomas, chordomas, dysgerminomas, nasopharyngeal tumours and metastases.
2. **Non-neoplastic masses** such as aneurysms, Rathke pouch cysts, fibrous dysplasia, sphenoidal sinus mucoceles and arachnoid cysts.
3. **Miscellaneous disorders** including demyelination, inflammation, trauma, radiation-induced necrosis and vasculitis.

Pituitary adenoma

Clinical features

The chromophobe adenoma is the most common primary intracranial tumour to produce neuro-ophthalmological features. Although generally detected by endocrinologists, non-secreting tumours may first present to ophthalmologists.

1. **Presentation** is typically during early adult life or middle age and only occasionally in the elderly with the following:
   a. ***Headache*** may be prominent due to involvement of pain-sensitive fibres in the diaphragma sellae. As the tumour expands upwards and breaks through the diaphragma the headaches may stop. The headache is non-specific and does not have the usual features associated with raised intracranial pressure. Diagnostic delay is therefore common in the absence of obvious endocrine disturbances.
   b. ***Visual symptoms*** usually have a very gradual onset and may not be noticed by the patient until well established. It is therefore essential to examine the visual function in all patients with non-specific headaches or endocrine disturbances.
2. **Visual field defects** depend on the anatomical relationship between the pituitary and chiasm.
   - If the chiasm is central, both superotemporal fields are affected first, as the tumour grows upwards and splays

the anterior chiasmal notch, compressing the crossing inferonasal fibres (Fig. 18.95).

- The defects then progress into the lower temporal fields. As tumour growth is often asymmetrical, the degree of visual field loss is usually different on the two sides.
- Patients may not present until central vision is affected from pressure on the macular fibres. The eye with the greater field loss usually also has more marked impairment of visual acuity.

NB: The absence of a visual field defect does not exclude a pituitary tumour, since tumours confined to the sella are often visually asymptomatic. Acidophil adenomas do not expand beyond the sella as frequently as chromophobe adenomas, and basophil adenomas are usually small and rarely compress the chiasm.

3. **Differential diagnosis** of bitemporal defects includes dermatochalasis of the upper eyelids, tilted discs (Fig. 18.96), optic nerve colobomas, nasal retinoschisis, nasal retinitis pigmentosa and functional visual loss.

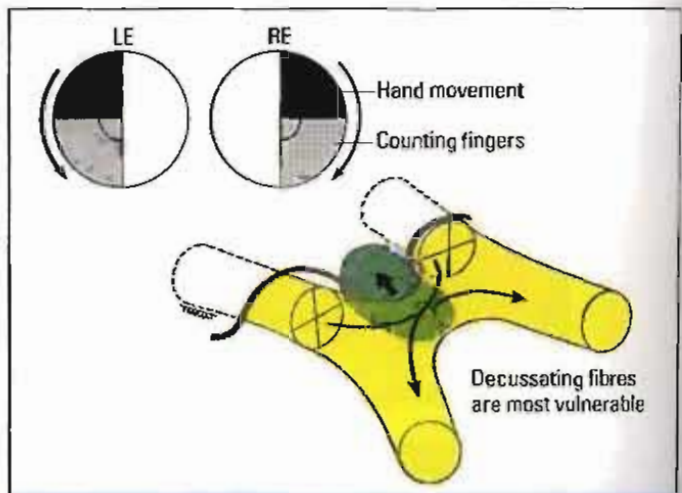


Fig. 18.95
Progression of bitemporal visual field defects caused by compression of the chiasm from below by a pituitary adenoma

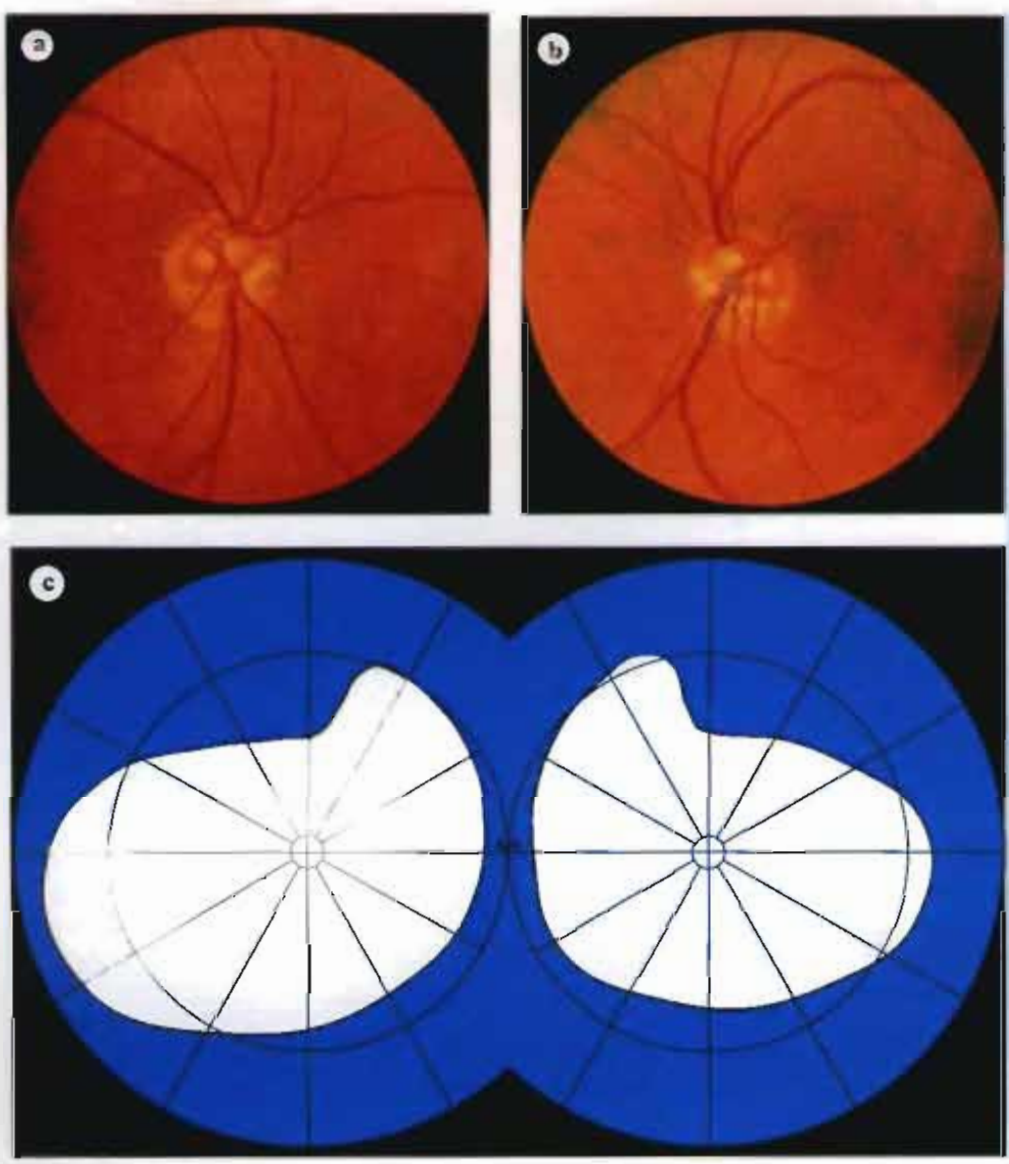


Fig. 18.96
(a and b) Tilted discs; (c) associated bitemporal visual field defects which do not respect the vertical midline
(Courtesy of Wilmer Institute)

4. **Colour desaturation** across the vertical midline of the uniocular visual field is an early sign of chiasmal compression which can be detected very simply with a red pin or a red Mydriacyl bottle top.
   - Each eye is tested separately.
   - The patient is asked to compare the colour and intensity of the target as it is brought from the nasal to the temporal visual field.
   - Another technique is to simultaneously present red targets in precisely symmetrical parts of the temporal and nasal visual fields, and to ask if the colours appear the same.
   - Patients may also miss the temporal number on Ishihara testing.
5. **Optic atrophy** is present in approximately 50% of cases with field defects caused by pituitary lesions. Patients are invariably more aware of difficulties with central vision (e.g. when reading) than with peripheral vision. It is therefore important to perform very careful visual field examinations on both eyes in patients with unexplained unilateral deterioration of central vision. When optic atrophy is present the prognosis for visual recovery after treatment is guarded. When nerve fibre loss is confined to fibres originating in the nasal retina (i.e. nasal to the fovea), only the nasal and temporal aspects of the disc will be involved, resulting in a band or 'bow-tie'-shaped atrophy.
6. **Miscellaneous features** include diplopia as a result of lateral expansion into the cavernous sinus and involvement of ocular motor nerves and, rarely, see-saw nystagmus of Maddox.
7. **Pituitary apoplexy** is a rare condition caused by a sudden increase in the size of a pituitary tumour, often secondary to haemorrhage.
   a. ***Presentation*** is with severe headache, diplopia, visual loss and photophobia.
   b. ***Signs*** include ophthalmoplegia, decreased sensation over the distribution of the first and second divisions of the trigeminal nerve and variable visual loss.
   c. ***Treatment*** with systemic steroids and surgery may be necessary to prevent blindness and other neurological complications.

Special investigations

1. **MRI** demonstrates the relationship between a mass lesion and the chiasm. The optimal study consists of coronal, axial and sagittal thin sections through the chiasm and optic nerves before and after gadolinium injection. The coronal plane is optimal for demonstrating sellar contents. Pituitary adenomas are typically hypointense on T1 images, hyperintense on T2 images and enhance strongly with gadolinium in a heterogeneous fashion (Fig. 18.97 and *see* Fig. 18.7). Repeated MRI to monitor progress is safe because there is no ionizing radiation risk.
2. **CT** will demonstrate enlargement or erosion of the sella.

Fig. 18.97
Sagittal T1-weighted gadolinium-enhanced MRI scan showing a pituitary adenoma (Courtesy of D. Thomas)

3. **Endocrinological** evaluation should be tailored to the individual patient. All patients suspected of having a pituitary adenoma should have assays of serum prolactin, FSH, TSH and growth hormone. An insulin stress test may also be required in selected cases. Patients with large adenomas with visual field defects are at some risk of pituitary apoplexy if the hypoglycaemic response is profound.

Treatment

Not all tumours require treatment; observation may be appropriate for incidentally discovered and clinically silent tumours.

1. **Medical** therapy to shrink a prolactin-secreting tumour involves dopamine agonists such as cabergoline or bromocriptine. Patients with significant visual field defects should have urgent prolactin level assay and, if elevated, treatment should be started as soon as possible. Visual function may improve within hours. Endocrine function also often improves with cessation of galactorrhoea, improvement of libido and return of menstruation.
2. **Surgery**
   a. ***Indications*** are mass effects causing severe compressive problems or failure to respond to medical therapy or radiotherapy.
   b. ***Technique***. Hypophysectomy is most frequently performed through a trans-sphenoidal approach through the upper gum under the lips. Occasionally both trans-sphenoidal hypophysectomy and a craniotomy are required to remove tissue above the diaphragma sellae.
   c. ***Visual recovery*** is triphasic.

- An early fast phase in the first week may lead to normalization of visual fields in some patients.
- A subsequent slow phase between 1 and 4 months is the period of most notable improvement.
- A late phase (6 months to 3 years) of mild improvement follows.

3. **Radiotherapy** is often used as an adjunct following incomplete removal of tumour. It can also be used as primary treatment in selected cases. While usually effective in preventing further tumour growth it is often less successful in controlling abnormal hormone secretion.
4. **Gamma knife** stereotactic radiotherapy is a relatively new method of delivering a concentrated dose of radiation to the tumour with little radiation to surrounding tissues. It is therefore of particular value in treating adenomas in close proximity to the optic nerve or when the cavernous sinus is invaded.

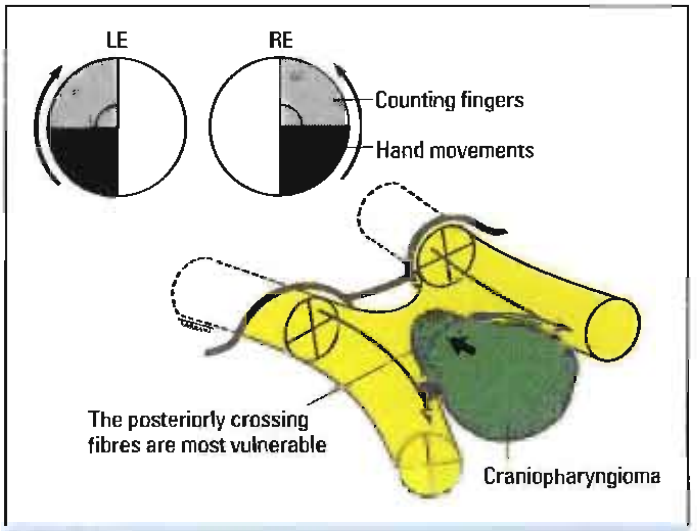


Fig. 18.98
Progression of bitemporal visual field defects caused by compression of the chiasm from above by a craniopharyngioma

Fig. 18.99
Sagittal T1-weighted MRI scan showing a craniopharyngioma
(Courtesy of K. Nischal)

Craniopharyngioma

The craniopharyngioma is a slow-growing tumour arising from vestigial remnants of Rathke pouch along the pituitary stalk.

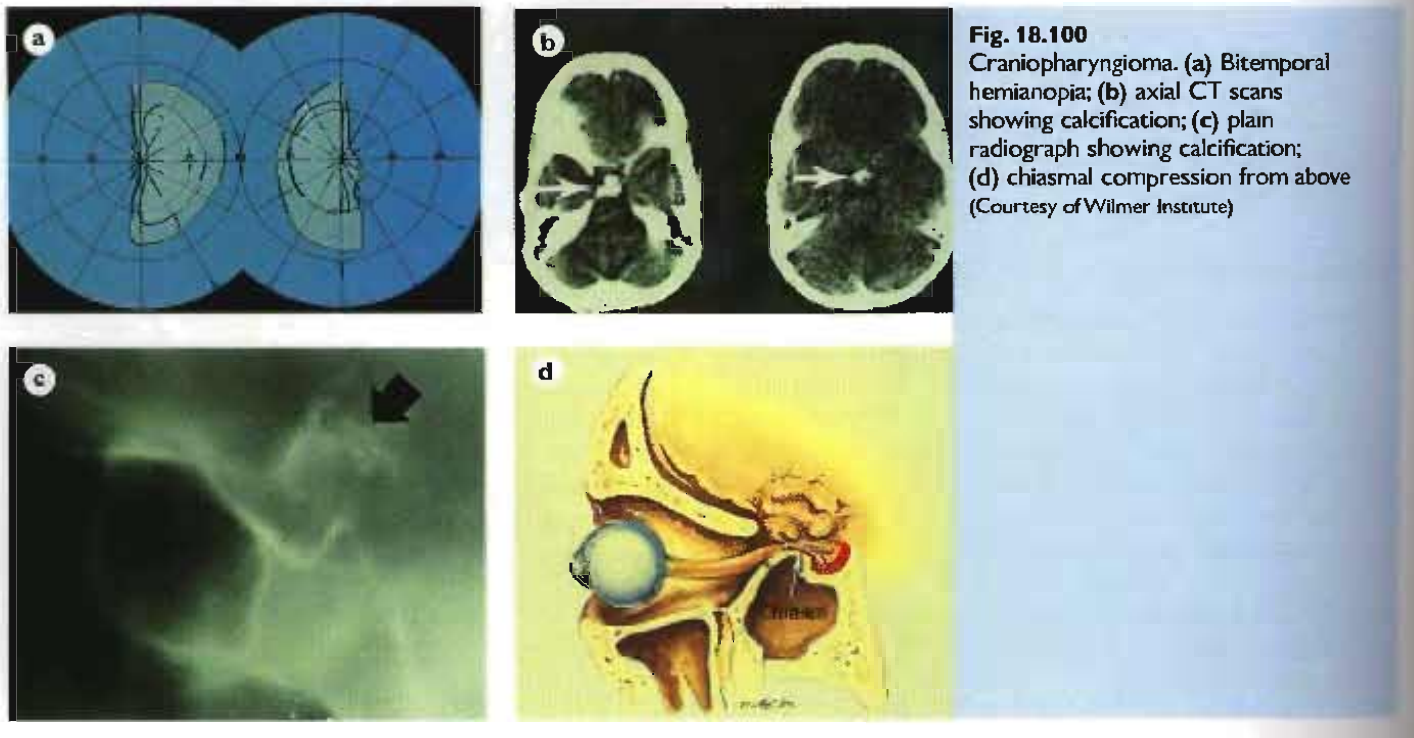


Fig. 18.100
Craniopharyngioma. (a) Bitemporal hemianopia; (b) axial CT scans showing calcification; (c) plain radiograph showing calcification; (d) chiasmal compression from above
(Courtesy of Wilmer Institute)

1. **Presentation** depends on the age of the patient:
   a. Children frequently present with dwarfism, delayed sexual development and obesity due to interference with hypothalamic function.
   b. Adults usually present with visual impairment and visual field defects.
2. **Visual field defects** are complex and may be due to involvement of the optic nerves, chiasm or tracts.
   - The initial defect frequently involves both inferotemporal fields because the tumour compresses the chiasm from above and behind, damaging the upper nasal fibres (Fig. 18.98).
   - The defects then spread to involve the upper temporal fields.
3. **MRI** shows the location of the tumour but not calcification which is present in 50–70% of cases. A solid tumour appears isointense on T1 images (Fig. 18.99). Cystic components appear hyperintense on T1 images.
4. **CT** (Fig. 18.100b) and plain films (Fig. 18.100c) demonstrate calcification but this is not diagnostic of craniopharyngioma because it may also be found in other parachiasmal lesions such as meningiomas, aneurysms and chordomas.
5. **Treatment** is mainly surgical, although intimacy to the chiasm may preclude complete removal. Postoperative radiotherapy may be helpful, but recurrences are common, necessitating lifelong follow-up.

Meningioma

Intracranial meningiomas typically affect middle-aged women. Visual field defects and clinical signs depend on the location of the tumour.

1. **Tuberculum sellae** meningiomas typically compress the junction of the chiasm with the optic nerve. This gives rise to an ipsilateral central scotoma caused by optic nerve

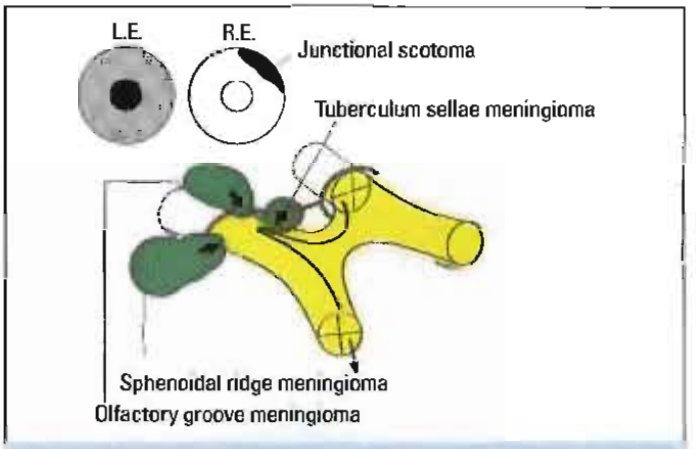


Fig. 18.101
Intracranial optic nerve compression by meningiomas and visual field defect caused by a tuberculum sellae meningioma

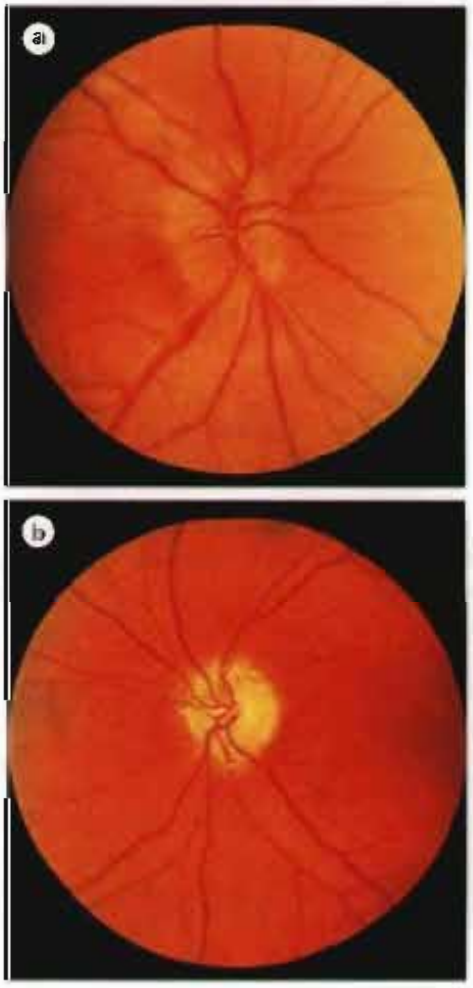


Fig. 18.102
Optic nerve compression by left sphenoidal ridge meningioma. (a) Disc swelling; (b) optic atrophy; (c) plain radiograph showing hyperostosis (arrows)
(Courtesy of Wilmer Institute)

compression and a contralateral upper temporal defect (junctional scotoma) due to damage to the anterior knee of Wilbrand (Fig. 18.101).

2. **Sphenoidal ridge** meningiomas compress the optic nerve early if the tumour is located medially and late if the lateral aspect of the sphenoid bone and middle cranial fossa are involved (Figs 18.102 and 18.103). A classic finding in the latter is fullness in the temporal fossa as a result of hyperostosis (Fig. 18.104).

Fig. 18.103
Axial T2-weighted MRI scan showing a left sphenoidal ridge meningioma (Courtesy of D. Thomas)

Fig. 18.104
Right sphenoidal ridge meningioma causing reactive hyperostosis and proptosis

3. **Olfactory groove** meningioma may cause loss of the sense of smell, as well as optic nerve compression.
4. **Treatment** is surgical but postoperative radiotherapy is frequently used in the event of incomplete excision.

Optic tract

Introduction

Retrochiasmal pathology results in binocular visual field defects involving contralateral visual space. Both eyes therefore manifest partial or total visual hemifield loss opposite the side of a retrochiasmal lesion. Such a 'hemianopia' involving the same side of visual space in both eyes is homonymous, in contradistinction to that seen in chiasmal compression, which produces heteronymous (bitemporal) hemianopia, in which opposite sides of the visual field are affected in each eye.

Incongruity

A homonymous hemianopia may be incomplete or complete. In the context of incomplete hemianopia, congruity refers to how closely the extent and pattern of field loss in one eye matches that of the other. Almost identical field defects in either eye are therefore highly congruous, while mismatching right and left visual field defects are incongruous. Hemianopia secondary to pathology in the anterior retrochiasmal visual pathways is characteristically incongruous, while that due to pathology further back (i.e. the posterior optic radiations) manifests a high degree of congruity.

Clinical features

1. **Homonymous hemianopia.** The optic tracts arise at the posterior aspect of the chiasm, diverge and extend posteriorly around the cerebral peduncles, to terminate in the lateral geniculate bodies. Each optic tract contains crossed fibres from the contralateral nasal hemiretina, and uncrossed fibres from the ipsilateral temporal hemiretina. Nerve fibres originating from corresponding retinal elements are, however, not closely aligned. Homonymous hemianopias caused by optic tract lesions are therefore characteristically incongruous (Fig. 18.105a). Lesions of the lateral geniculate body also produce asymmetrical hemianopic defects. The causes of optic tract disease are similar to those affecting the chiasm but the tract is particularly vulnerable when the chiasm is pre-fixed.
2. **Wernicke hemianopic pupil.** The optic tracts contain both visual and pupillomotor fibres. The visual fibres terminate in the lateral geniculate body but the pupillary

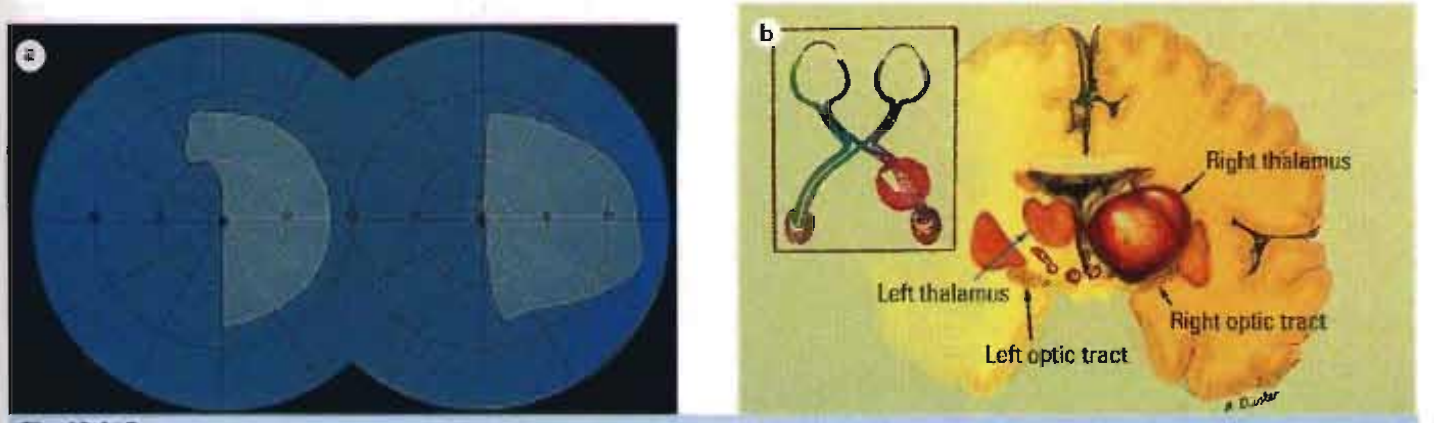


Fig. 18.105
Optic tract lesion. (a) Incongruous homonymous hemianopia; (b) location of lesion (Courtesy of Wilmer Institute)

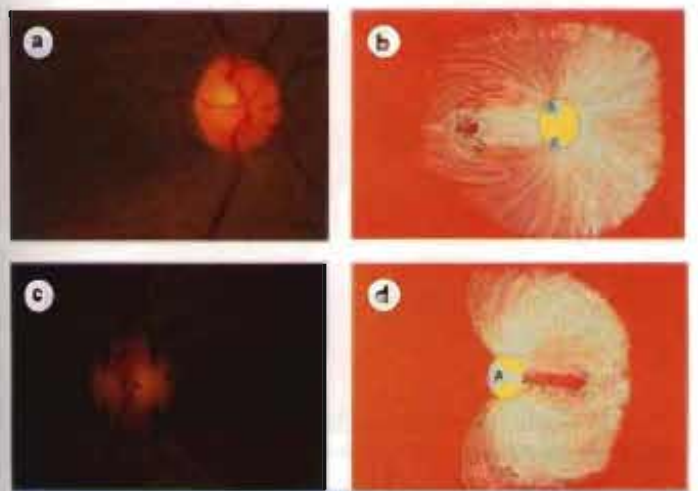


Fig. 18.106
Optic atrophy due to a right optic tract lesion. (a and b) Ipsilateral eye; (c and d) contralateral eye (see text) (Courtesy of Wilmer Institute)

fibres leave the optic tract anterior to the lateral geniculate body, projecting through the brachium of the superior colliculus to terminate in the pretectal nuclei. An optic tract lesion may therefore give rise to an afferent pupillary conduction defect. Characteristically, the pupillary light reflex will be normal when the unaffected hemiretina is stimulated, and absent when the involved hemiretina is stimulated (i.e. light is shone from the hemianopic side). In practice, this Wernicke hemianopic pupillary reaction is difficult to elicit because of scatter of light within the eye; hence the need for a very fine beam of light.

3. **Optic atrophy** may result when the optic tracts are damaged because the fibres in the optic tract are the axons of the retinal ganglion cells. The ipsilateral disc manifests atrophy of the superior and inferior aspects of the neuroretinal rim (fibres from the temporal retina) (Fig. 18.106a and b), while the contralateral disc manifests a bow-tie pattern of atrophy (nasal retinal fibres) (Fig. 18.106c and d).
4. **Contralateral pyramidal signs** may occur when an optic tract lesion also damages the ipsilateral cerebral peduncle.

Optic radiations

Applied anatomy

The optic radiations extend from the lateral geniculate body to the striate cortex, which is located on the medial aspect of the occipital lobe, above and below the calcarine fissure (Fig. 18.107). The optic radiations and visual cortex have a dual blood supply from the middle and posterior cerebral arteries. As the radiations pass posteriorly, fibres from corresponding retinal elements lie progressively closer together. For this reason, incomplete hemianopias caused by lesions of the posterior radiations are more congruous than those involving the anterior radiations. Because these fibres are third-order neurones that originate in the lateral geniculate body, lesions of the optic radiations do not produce optic atrophy.

Temporal radiations

1. **Visual field defect** consists of a contralateral, homonymous, superior quadrantanopia ('pie in the sky'), because the inferior fibres of the optic radiations, which subserve the upper visual fields, first sweep antero-inferiorly into the temporal lobe (Meyer loop) around the anterior tip of the temporal horn of the lateral ventricle (Fig. 18.107a).
2. **Associated features** include contralateral hemisensory disturbance and mild hemiparesis, because the temporal radiations pass very close to the sensory and motor fibres of the internal capsule before passing posteriorly and rejoining the superior fibres. Other features of temporal lobe disease include paroxysmal olfactory and gustatory hallucinations (uncinate fits), formed visual hallucina-

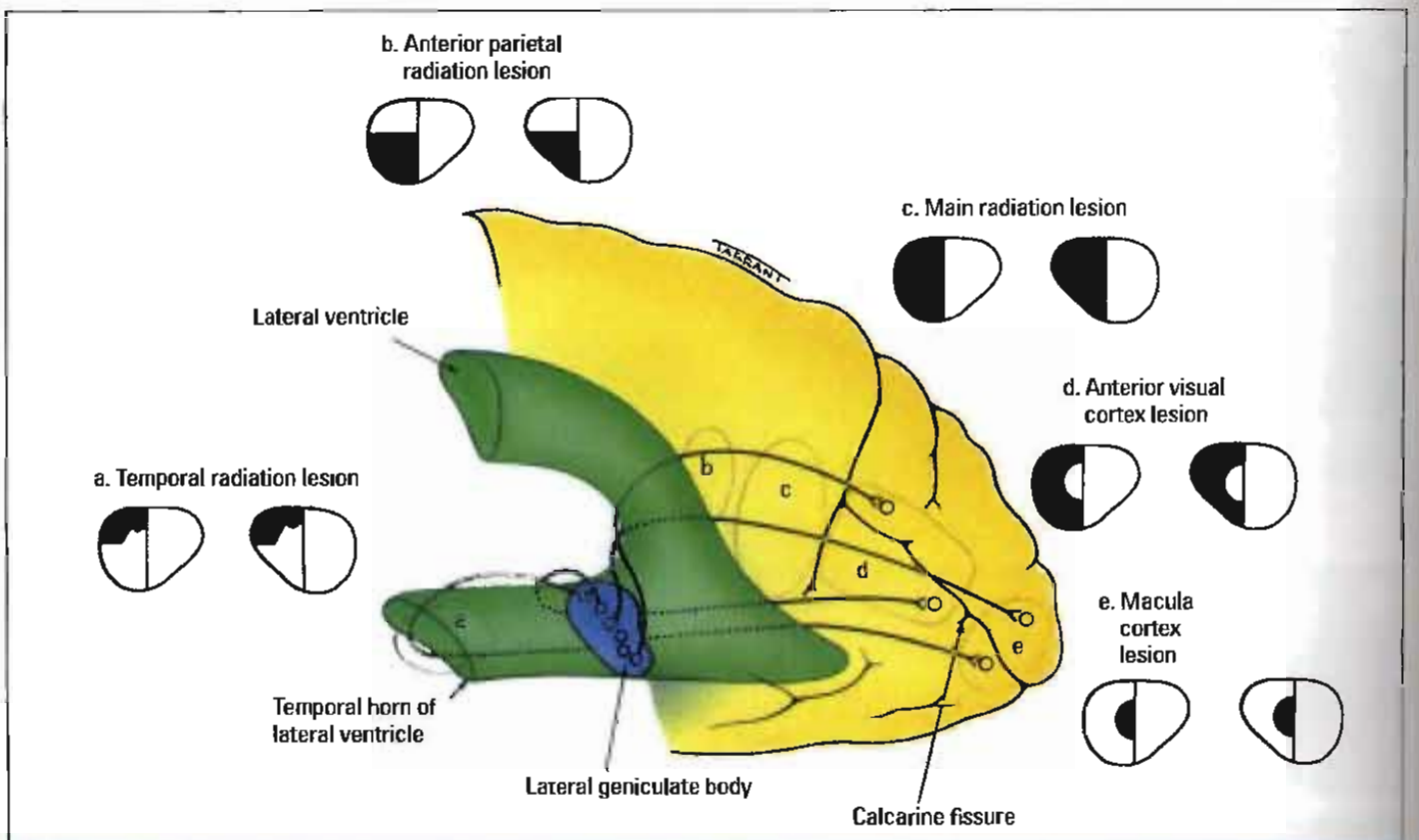


Fig. 18.107
Visual field defects caused by lesions of the optic radiations and visual cortex

tions, seizures and receptive dysphasia if the dominant hemisphere is involved.

Anterior parietal radiations

1. **Visual field defect** consists of a contralateral, homonymous, inferior quadrantanopia ('pie on the floor') because the superior fibres of the radiations, which subserve the inferior visual fields, proceed directly posteriorly through the parietal lobe to the occipital cortex. A lesion involving only the anterior parietal part of the radiations is, however, very rare. In general, hemianopias resulting from parietal lobe lesions tend to be relatively congruous (Fig. 18.107b).
2. **Associated features** of parietal lobe disease include agnosias, visual perception difficulties (particularly with right parietal lesions), right–left confusion and acalculia (particularly with left parietal lesions).

Main radiations

Deep in the parietal lobe, the optic radiations lie just external to the trigone and the occipital horn of the lateral ventricle. Lesions in this area usually cause a complete homonymous hemianopia (Fig. 18.107c). Optokinetic nystagmus (OKN) may be useful in localizing a lesion causing an isolated homonymous hemianopia that does not conform to any set pattern in a patient without associated neurological deficits. Normally OKN involves smooth pursuit of a target, followed by a saccade in the opposite direction to fixate on the next target. If the optomotor pathways in the posterior hemisphere are damaged, the OKN response will be diminished when targets are rotated towards the side of the lesion (i.e. away from the hemianopia). This is explained on the basis that the occipital lobe can no longer control ipsilateral pursuit, while the contralateral hemianopia inhibits refixational saccades. This is called the positive OKN sign. The combination of a homonymous hemianopia and OKN asymmetry therefore suggests a lesion involving the posterior optic radiations. Rarely occipital lobe lesions may also cause OKN asymmetry.

Striate cortex

Clinical features

1. **Visual field defects.** In the striate cortex the peripheral visual fields are represented anteriorly. This part of the occipital lobe is supplied by a branch of the posterior cerebral artery. Central macular vision is represented posteriorly just lateral to the tip of the calcarine cortex, an area supplied mainly by a branch of the middle cerebral artery. Occlusion of the posterior cerebral artery will therefore tend to produce a macular-sparing congruous homonymous hemianopia (Fig. 18.107d). Damage to the tip of the occipital cortex, as might occur from a head

injury, tends to give rise to congruous, homonymous, macular defects, although asymmetrical macular sparing may sometimes occur with vascular lesions of the occipital lobe.

NB: The anterior-most part of the calcarine cortex subserves the temporal extremity of the visual field of the contralateral eye, the area of visual space that extends beyond the field of binocular single vision and is perceived monocularly. A lesion in this area may therefore give rise to a monocular temporal field defect in the contralateral eye, known as a temporal crescent.

2. **Associated features** of visual cortex disease (cortical blindness) are: (a) formed visual hallucinations, particularly involving the hemianopic field, (b) denial of blindness (Anton syndrome) and (c) Riddoch phenomenon, characterized by the ability to perceive kinetic, but not static targets.

Causes

1. **Vascular lesions** in the territory of the posterior cerebral artery are responsible for over 90% of isolated homonymous hemianopias with no other neurological deficits.
2. **Other causes**, which are less common, include migraine, trauma and primary or metastatic tumours.

Higher visual function

From the striate cortex (area 17), visual information is relayed to the visual association areas (18 and 19) of the cerebral cortex, where it is processed, analysed and interpreted. Lesions of various areas of the cerebral cortex produce characteristic clinical pictures.

Alexia and agraphia

The angulate gyrus of the dominant hemisphere (commonly the left) subserves the ability to write. Visual information from both occipital cortices is relayed to the left angulate gyrus, fibres from the right side crossing the midline in the splenium of the corpus callosum. Alexia (the inability to read), commonly accompanied by agraphia (the inability to write), may be produced by lesions of the angulate gyrus of the dominant cerebral hemisphere. Alexia may occur independently of agraphia in the context of a left occipital lesion of sufficient magnitude to involve fibres crossing the splenium, from the right occipital cortex to the left angulate gyrus. The clinical features consist of a right homonymous hemianopia with alexia, since information from the right occipital cortex (left visual field) is prevented from reaching the left angulate gyrus.

NB: It is therefore mandatory to examine reading ability in the context of a right hemianopia.

Agnosia

Lesions of the inferior occipitotemporal area may produce a wide range of clinical features. Bilateral disease may produce visual agnosia—the inability to recognize objects by sight—while the ability to recognize by touch is retained. Prosopagnosia implies the inability to recognize and distinguish between faces. Colour vision too has its seat in this area, each half of the visual field being represented contralaterally. Lesions here may therefore also result in contralateral (cerebral) hemi-achromatopsia with total loss or relative desaturation of colour.

Visual hallucinations

Significant visual impairment due to pathology anywhere along the visual pathway, from the eye to the primary visual cortex, may result in the emergence of complex visual hallucinations. This condition (Charles Bonnet syndrome) is thought to represent a release phenomenon, secondary to deafferentation of the visual association areas, which then exhibit spontaneous activity, with resultant complex (formed) visual hallucinations. Such hallucinations are often brilliantly clear and detailed, in contrast to the patient's normally indistinct vision, and are recognized by the patient as unreal, often after initial deception. Hallucinatory content is usually pleasant but may be distressing. Patients aware of the unreality of their visions often do not admit their existence for fear of being labelled insane. Sensitive history taking and reassurance are usually sufficient.

Migraine

Clinical features

Migraine is an often familial disorder, more common in females, characterized by recurrent attacks of headache widely variable in intensity, duration and frequency. The headache is commonly unilateral, associated with nausea and vomiting, and may be preceded by or associated with neurological and mood disturbances. However, all these characteristics are not necessarily present during each attack or in every patient. The main types of migraine are as follows.

Common migraine

Common migraine (migraine without aura) is characterized by headache with autonomic nervous system dysfunction (e.g. pallor and nausea), but without stereotypical neurological or ophthalmic features as in classical migraine (*see* later).

- Premonitory features include changes in mood, frequent yawning or other non-specific prodromal symptoms such as poor concentration.
- The headache starts anywhere on the cranium and is pounding or throbbing. It usually spreads to involve one

Fig. 18.108
Progression of classic migrainous fortification spectrum and scintillating scotoma

half or even the whole head. If retro-orbital, the pain may be mistaken for ocular or sinus disease.

- During the attack, which lasts from hours to a day or more, the patient is frequently photophobic and phonophobic and seeks relief in a quiet, dark environment or through sleep.
- Because of the absence of the well-known migrainous visual distortions, severe nausea and vomiting, common migraine often goes unrecognized.

Classical migraine

Classical migraine (migraine with aura) is less common but better recognized (Fig. 18.108).

- The attack is heralded by a visual aura which lasts about 20 minutes. This may consist of bright or dark spots, zigzags, heat haze distortions, jig-saw puzzle effects, scintillating scotomata, tunnel vision or fortification spectra, which may progress to homonymous hemianopia.
- A small bright positive paracentral scotoma develops, lined on one side with luminous zig-zag lines.
- After several minutes the fortification spectrum gradually enlarges with the open end pointing centrally. It is often lined on the inner edge by an absent area of vision (negative scotoma).
- As the scotoma expands it may drift towards the temporal periphery before breaking up.

NB: These visual features, supposedly pathognomonic of migraine, may rarely be caused by degenerative arterial disease in the occipital poles.

- The headache follows the aura and is usually hemicranial, opposite the hemianopia and is accompanied by nausea and photophobia. It may, however, be absent, trivial or very severe, with considerable variation between attacks even in the same individual.

Cluster headache

Cluster headache (migrainous neuralgia) is a migraine variant which typically affects men during the fourth and fifth decades of life. It is of particular interest to ophthalmologists because it is associated with ocular features and may initially be misdiagnosed as an ocular problem. The condition is characterized by a stereotyped headache accompanied by various autonomic phenomena occurring almost every day for a period of some weeks.

- The headache is unilateral, oculotemporal, excruciating, sharp and deep.
- It begins relatively abruptly, lasts between 10 minutes and 2 hours, and then clears quickly.
- It may occur several times in a 24-hour period, often at particular times, not infrequently at around 2 a.m.
- Once the 'cluster' is over, there may be a long headache-free interval of several years.
- Associated autonomic phenomena include lacrimation, conjunctival injection and rhinorrhoea.

NB: Cluster headaches are also a common cause of a transient or permanent postganglionic Horner syndrome.

Other types of migraine

1. **Focal migraine** is characterized by transient dysphasia, hemisensory symptoms or even focal weakness in addition to other symptoms of migraine.
2. **Migraine sine migraine** is characterized by episodic visual disturbances without headache. Elderly patients with a past history of classical migraine are typically affected.
3. **Retinal migraine** is characterized by acute, transient, unilateral loss of vision. Since this may occur in middle-aged patients without past history of migraine, it is prudent to investigate such individuals as undergoing attacks of retinal embolization, until proved otherwise.
4. **Ophthalmoplegic migraine** is rare and typically starts before the age of 10 years. It is characterized by a recurrent transient third nerve palsy which begins after the headache.
5. **Familial hemiplegic migraine** is characterized by a failure of full recovery of focal neurological features after an attack of migraine subsides.
6. **Basilar migraine** occurs in children. It is characterized by a typical migrainous aura associated with numbness and tingling of the lips and extremities which is often bilateral. Ataxia of gait and speech also occur, with occasional impairment of consciousness.

Management

1. **General measures** include the elimination of conditions and agents that may precipitate an attack of migraine, such as coffee, chocolate, alcohol, cheese, oral contraceptives, stress, lack of sleep and long intervals without food.
2. **Prophylaxis** is indicated if the frequency and/or severity of the attacks are beyond the patient's tolerance. This may involve beta-adrenergic blockers, calcium channel blockers, amitriptyline, clonidine, pizotifen and low-dose aspirin.
3. **Treatment** of an acute attack may be with simple analgesics (aspirin, codeine analogues, paracetamol or a NSAID) and, if appropriate, an anti-emetic such as metoclopramide. Other drugs, usually reserved for patients refractory to analgesics, include sumatriptan and ergotamine tartrate.

Differential diagnosis

Visual phenomena

The visual phenomena of migraine are typically binocular, zig-zag, scintillating and migrate within the visual field. This is often followed by a scotoma and/or homonymous visual loss. The patient may report loss of vision in the eye ipsilateral to the hemianopia. The following conditions should be considered in the differential diagnosis:

1. **Acute posterior vitreous detachment** is characterized by photopsia, usually associated with the sudden onset of floaters. The flashing lights are usually projected into the temporal visual field and may be precipitated by movements of the head or eyes.
2. **Transient ischaemic attacks** due to retinal microembolization are unilateral and not scintillating. The patient often describes a 'shade' or 'cloud' which typically starts in the upper or lower parts of the visual field and spreads centrally. It lasts several minutes and clears from the centre to the periphery.
3. **Transient visual obscurations** last only a few seconds and are characterized by a 'greying out' or 'darkening' of vision in one or both eyes. They classically occur in patients with papilloedema and are often precipitated by changes in posture. They may also precede anterior ischaemic optic neuropathy in patients with giant cell arteritis.

Neuralgias

The following conditions should be considered in the differential diagnosis of ocular or periocular pain in the absence of apparent physical disease:

1. **Herpes zoster ophthalmicus** frequently presents with pain 2–3 days before the onset of the characteristic vesicular rash.
2. **Trigeminal neuralgia** is characterized by brief attacks of severe pain that start in the distribution of one of the divisions of the trigeminal nerve. The pain is paroxysmal and sharp, like an electric shock, usually occurring in multiple bursts lasting a few seconds, in rapid succession. Facial sensation is normal. Treatment involves antiepileptic drugs such as carbamazepine, phenytoin and sodium valporate. Trigeminal neuralgia of compressive aetiology may necessitate intracranial surgical decompression of the trigeminal nerve.
3. **Raeder paratrigeminal neuralgia** occurs in middle-aged men. It is characterized by severe unilateral headache with periocular pain in the distribution of the first division of the trigeminal nerve associated with an ipsilateral Horner syndrome. The pain may last from hours to weeks before it resolves spontaneously.
4. **Greater occipital neuralgia** is characterized by attacks of pain that begin in the occipital region and then spread to the eye, temple and face. The attacks frequently occur at night and are associated with flushing of the face, dizziness and sometimes ipsilateral nasal obstruction. Examination during an attack may reveal extreme tenderness between the mastoid process and occipital protuberance.
5. **Ophthalmodynia periodica** is characterized by short, sharp stabbing ocular pain which often causes the patient to place the hand over the involved eye. A second series of episodes may immediately follow the initial attack.
6. **Ice-pick syndrome** is characterized by attacks of momentary, multifocal, sharp pain around the skull, face and eyes. Unlike trigeminal neuralgia there are no specific trigger points; the pain also does not conform to the anatomical distribution of the trigeminal nerve. Facial pain in a young person may occasionally be a manifestation of multiple sclerosis.

Intracranial aneurysms

Applied anatomy

The arterial supply to the brain comes from the internal carotid and vertebral arteries.

1. **The vertebral** arteries enter the cranial cavity through the foramen magnum and unite into the basilar artery, which ascends on the ventral surface of the brain stem. After giving rise to branches to the brain stem, the basilar artery divides into its terminal branches: the posterior cerebral arteries.
2. **The internal carotid** arteries enter the base of the skull through the carotid canal and the cranial cavity through the foramen lacerum, at the apex of the petrous part of the temporal bone. They then run forwards in the cavernous sinus, lateral to the pituitary gland before ascending, lateral to the optic chiasm and dividing into the anterior and middle cerebral arteries.
3. **The circle of Willis**. The anterior cerebral arteries are connected by the anterior communicating artery. The middle and posterior cerebral arteries are connected by the posterior communicating artery (Fig. 18.109). This anastomosis forms the circle of Willis, which lies in the subarachnoid space on the ventral surface of the brain.

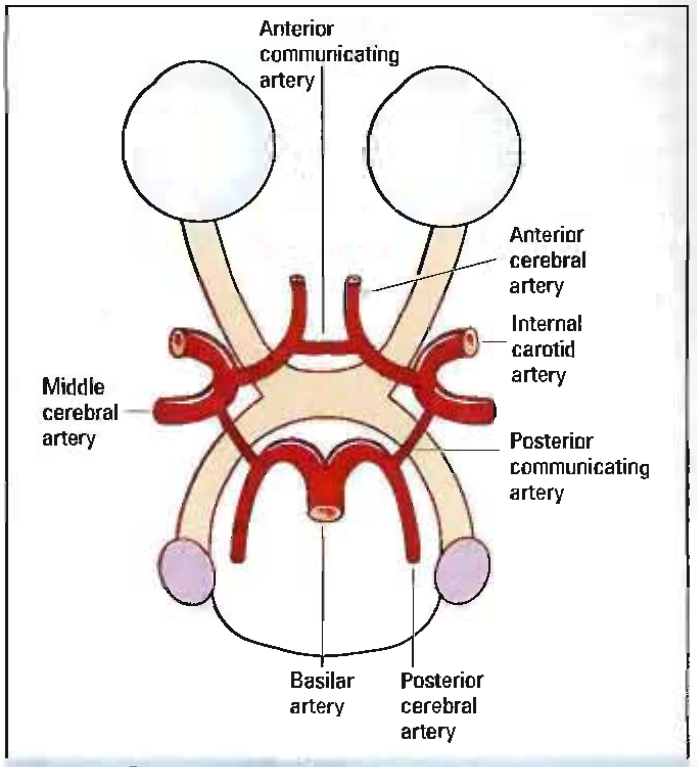


Fig. 18.109
Dorsal view of the circle of Willis (Courtesy of G. Robertson)

Neurological considerations

Intracranial aneurysms are saccular arterial outpouchings that most commonly develop at the branching points of the major arteries coursing through the subarachnoid space at the base of the brain. Eighty-five per cent arise from the anterior half of the circle of Willis. Their prevalence ranges from 1% to 6% among adults in large autopsy series. Aneurysms are multiple (usually two or three) in about 25% of cases. The majority of aneurysms remain asymptomatic during life.

Complications

1. **Subarachnoid haemorrhage** due to rupture is by far the most frequent complication. This life-threatening event presents with sudden onset of severe headache, photophobia, clouding consciousness, vomiting and signs of meningeal irritation, including neck stiffness and positive Kernig sign. Blood-stained CSF is revealed on lumbar puncture. Approximately 12% of patients die before receiving medical attention. 40% of hospitalized patients die within 1 month and more than one-third of those that survive suffer major neurological deficits.
2. **Pressure effects** are less frequent and associated with 'giant' aneurysms (larger than 25 mm). The most common symptom is headache; associated signs depend on the location of the lesion and are frequently neuro-ophthalmological, such as third nerve palsy from aneurysm of the posterior communicating artery. Such 'giant' aneurysms also have a high subsequent rupture rate with an estimated frequency of 6% per year. The interval between warning mass signs and rupture varies from 1 day to 4 months, so that early diagnosis is paramount.

Fig. 18.110
Arteriogram with subtraction showing a small posterior communicating aneurysm (arrow) (Courtesy of S. Cudlip)

Neuroimaging

MRI (*see* Fig. 18.9), MRA or conventional (intra-arterial) angiography (Fig. 18.110) are useful in diagnosis. While the first two are capable of demonstrating large to medium-sized aneurysms, they often fail to detect those smaller than 5 mm. Despite infrequent but potentially serious risks including vascular damage and permanent neurological deficits, conventional angiography is still the 'gold standard', particularly prior to surgical intervention.

Treatment

Definitive treatment is surgical, aimed at excluding the aneurysmal sac from the intracranial circulation while preserving the parent artery. This involves placing a clip around the neck of the aneurysm or less frequently the insertion of soft metallic coils within the lumen of the aneurysm.

Neuro-ophthalmic aspects

Ocular motor nerve palsies

1. **Isolated third nerve palsy** may be caused by compression by an aneurysm of the posterior communicating artery at its junction with the internal carotid artery in the subarachnoid space (*see* Fig. 18.77). Presentation is typically with ipsilateral frontal headache and a total third nerve palsy (with internal ophthalmoplegia).

> ***NB:*** Pupil sparing in a total third nerve palsy almost always excludes an aneurysm. Pain is rarely absent; however, its absence does not exclude an aneurysm.

2. **Isolated sixth nerve palsy** can occur with aneurysms of the intracavernous part of the internal carotid artery, but very rarely from involvement in the subarachnoid space.

3. **Combined palsies** of the third and sixth nerves occur with intracavernous carotid aneurysms, although this may also occur in other cavernous sinus lesions. The fourth nerve may also be involved but this is frequently obscured by the other lesions. Although parasympathetic innervation is commonly damaged, mydriasis may not occur; the pupil may even be miosed because of coexistent damage to the sympathetic fibres.

NB: An important sign of cavernous sinus lesions is sensory loss over the distribution of the first division of the trigeminal nerve.

Visual loss

1. **Monocular** visual loss is most frequently caused by compression of the intracranial part of the optic nerve by aneurysms arising from the internal carotid artery near the origin of the ophthalmic artery, at its terminal bifurcation (*see* Fig. 18.93). The clinical picture is that of unilateral acute or progressive visual loss occasionally associated with orbital pain, which may initially be misdiagnosed as retrobulbar neuritis.
2. **Visual field defects** involving the nasal field may be caused by a giant aneurysm at or near the origin of the ophthalmic artery. Rarely, a giant aneurysm may compress the lateral aspect of the chiasm and cause a nasal field defect which is initially unilateral but may become bilateral if the chiasm is pushed across against the opposite carotid artery. Homonymous defects and cortical blindness may be caused by transient or permanent ischaemia of the retrochiasmal visual pathways.

NB: Carotid aneurysms may also invade the sella and mimic pituitary adenomas.

Terson syndrome

Terson syndrome refers to the combination of intraocular haemorrhage and subarachnoid haemorrhage due to aneurysmal rupture, most commonly arising from the anterior communicating artery. However, intraocular haemorrhage may also occur with subdural haematoma and acute elevation of intracranial pressure from other causes. The haemorrhage is frequently bilateral, and typically intraretinal or preretinal (subhyaloid) (Fig. 18.111) although occasionally subhyaloid blood may break into the vitreous. It is probable that intraocular bleeding is due to retinal venous stasis secondary to increase in cavernous sinus pressure. Vitreous haemorrhage usually resolves spontaneously within a few months and the long-term visual prognosis is good in the majority of cases. Early vitrectomy may be considered for dense bilateral vitreous involvement.

NB: Papilloedema may be a feature of subarachnoid haemorrhage. Elevation of intracranial pressure may be caused by blockage of CSF flow within the ventricular system (obstructive hydrocephalus) or defective CSF absorption by the arachnoid villi.

Myasthenia gravis

Myasthenia gravis is an uncommon autoimmune disorder, characterized by weakness and fatiguability of voluntary musculature. The condition affects females twice as commonly as males. Diagnostic tests include the edrophonium test, serum acetylcholine receptor antibody levels and electromyography. Myasthenia gravis may be (a) *ocular*, (b) *bulbar* or (c) *generalized* (*see* Chapter 20).

Ocular features

Ocular involvement occurs in 90% of cases and is the presenting feature in 60%. It is characterized by the following:

1. **Ptosis** is insidious, bilateral and frequently asymmetrical.
   - It is worse at the end of the day and least on awakening.
   - Ptosis is worse on prolonged upgaze due to fatigue.
   - If one eyelid is elevated manually as the patient looks up, the fellow eyelid will show fine oscillatory movements.
   - Cogan twitch sign is a brief upshoot of the eyelid as the eyes saccade from depression to the primary position.
   - Positive ice test: the degree of ptosis improves after an ice pack is placed on the eyelid for 2 minutes. The test is negative in non-myasthenic ptosis.
2. **Diplopia** is frequently vertical, although any or all of the extraocular muscles may be affected. A pseudo-

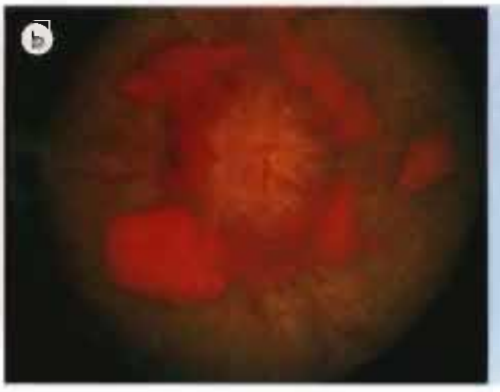


Fig. 18.111
Terson syndrome. (a) Intraretinal haemorrhages and a large subhyaloid haemorrhage; (b) oedematous optic disc surrounded by subhyaloid haemorrhages (Courtesy of Wilmer Institute)

internuclear ophthalmoplegia may be seen. Patients with stable deviations may benefit from muscle surgery, botulinum toxin injection or a combination of both.

3. **Nystagmoid movements** may be present on extremes of gaze.

Edrophonium test

Edrophonium is a short-acting anticholinesterase which increases the amount of acetylcholine available at the neuromuscular junction. In myasthenia this results in transient improvement of symptoms and signs such as weakness, ptosis and diplopia. The estimated sensitivity is 85% in ocular and 95% in systemic myasthenia. Potential but uncommon complications include bradycardia, loss of consciousness and even death. The test should therefore never be performed without an assistant, and a resuscitation trolley should also be close at hand in case of sudden cardiorespiratory arrest. The test is performed as follows:

1. Objective baseline measurements are made of the ptosis or diplopia with a Hess test (*see* Chapter 16).
2. Intravenous injection of atropine 0.3 mg is given to minimize muscarinic side effects.
3. Intravenous test dose of 0.2 ml (2 mg) edrophonium hydrochloride is given. If definite symptomatic improvement is noted the test is terminated forthwith.
4. The remaining 0.8 ml (8 mg) is given after 60 seconds, provided there is no hypersensitivity.
5. Final measurements/repeat Hess testing are made and the results compared, remembering that the effect lasts only 5 minutes (Fig. 18.112).

Chronic progressive external ophthalmoplegia

Chronic progressive external ophthalmoplegia (CPEO) refers to a group of disorders characterized by the triad of ptosis, slowly progressive bilateral ocular immobility and ragged-red fibre myopathy (Fig. 18.113d).

Classification

1. **Isolated** presents in adult life and is the mildest.
2. **Oculopharyngeal dystrophy** is of intermediate severity and presents in adolescence or early childhood. It is characterized by weakness of the pharyngeal muscles and wasting of the temporalis.
3. **Kearns–Sayre syndrome**, the most severe, presents in childhood and is associated with pigmentary retinopathy (Fig. 18.113c) and heart block (*see* Chapter 20).

Clinical features

1. **Ptosis**, usually the first sign, is bilateral and asymmetrical (Fig. 18.113a). Surgical correction may improve compensatory head posture but does not restore normal movements and is associated with a risk of corneal exposure.
2. **External ophthalmoplegia** begins in young adulthood and typically is symmetrical. It is characterized by a progressive course without remission or exacerbation. Initially upgaze is involved (Fig. 18.113b); subsequently lateral gaze is affected so that the eyes may become virtually fixed. A minority of patients with diplopia may benefit from surgery.

Essential blepharospasm

Clinical features

Essential blepharospasm is an uncommon but distressing idiopathic disorder which presents in the sixth decade and affects women more commonly than men by a 3:1 ratio. It is characterized by progressive involuntary spasm of the orbicularis oculi and upper facial muscles. In severe cases blepharospasm is disabling because it may temporarily render the patient functionally blind (Fig. 18.114a). Spasms may be precipitated by reading, driving, stress or bright light, and alleviated by talking, walking and relaxation.

Fig. 18.112
Positive edrophonium test in myasthenic ptosis. (a) Prior to injection; (b) 2 minutes after injection

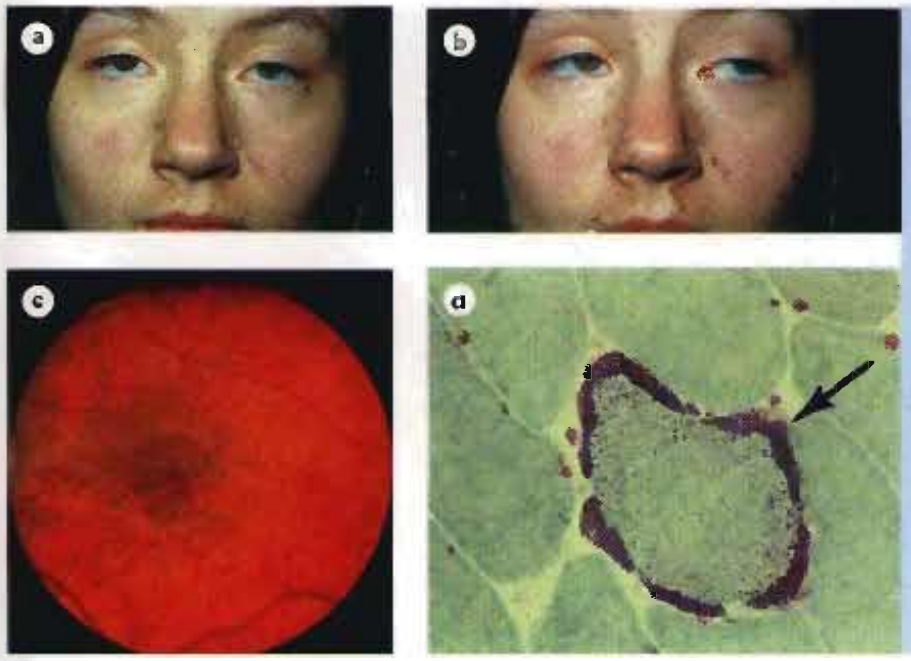


Fig. 18.113
Kearns–Sayre syndrome. (a) Symmetrical ptosis; (b) ophthalmoplegia; (c) pigmentary retinopathy; (d) histology showing ragged-red muscle fibre (arrow) (Courtesy of Wilmer Institute)

Fig. 18.114
Essential blepharospasm. (a) During attack; (b) after attack

1. **Meige syndrome** is a combination of blepharospasm and involvement of the lower facial and neck muscles.
2. **Breughel syndrome** is associated with severe mandibular and cervical muscle involvement.

Fig. 18.115
Botulinum toxin injection for essential blepharospasm

Treatment

Prior to commencing treatment it is important to exclude reflex blepharospasm, most commonly due to ocular surface disease such as filamentary keratitis.

1. **Medical** treatment with a great variety of drugs has been reported to ameliorate specific types of blepharospasm, but their efficacy is disappointing.
2. **Botulinum toxin** injected along the upper and lower eyelid and eyebrow affords temporary relief in most patients (Fig. 18.115). By interference with acetylcholine release from nerve terminals it results in temporary paralysis of the injected muscles. Most patients require repeat injections every 3–4 months; progressively larger doses may be needed. Side effects include lagophthalmos and ectropion or entropion, depending on the tone of the eyelids before the injection. Accidental migration of the toxin into the orbit may result in ptosis and diplopia due to paralysis of the levator or extraocular muscles.
3. **Surgical** treatment involves removal of the entire orbicularis, corrugator and procerus muscles. Such radical surgery is reserved for patients who cannot tolerate or are unresponsive to botulinum toxin.

Neurofibromatosis

Neurofibromatosis is a hereditary disorder that primarily affects cell growth of neural tissues. Inheritance is AD with irregular penetrance and variable expressivity. The mutation rate is high. The two main types are: (a) *type 1 (NF-1)* and (b) *type 2 (NF-2)*.

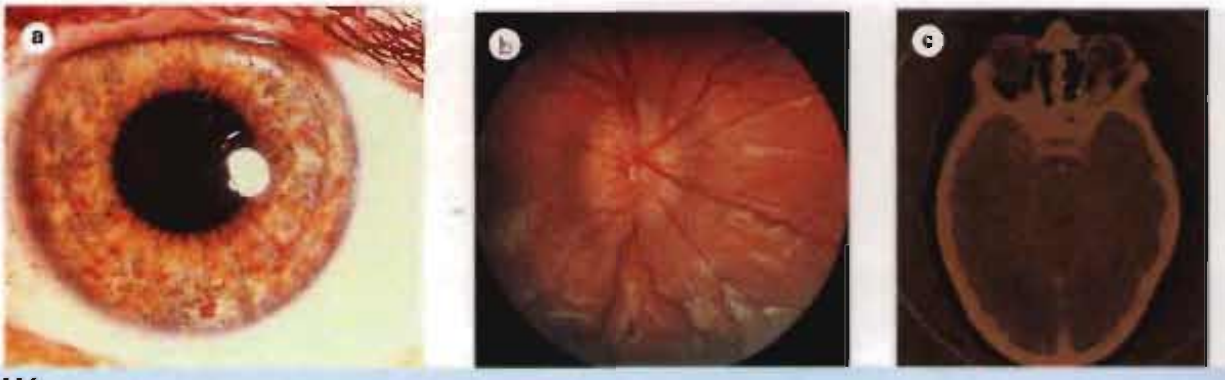


Fig. 18.116
NF-1. (a) Lisch nodules; (b) disc oedema due to optic nerve glioma; (c) CT scan showing optic nerve glioma (Courtesy of Wilmer Institute)

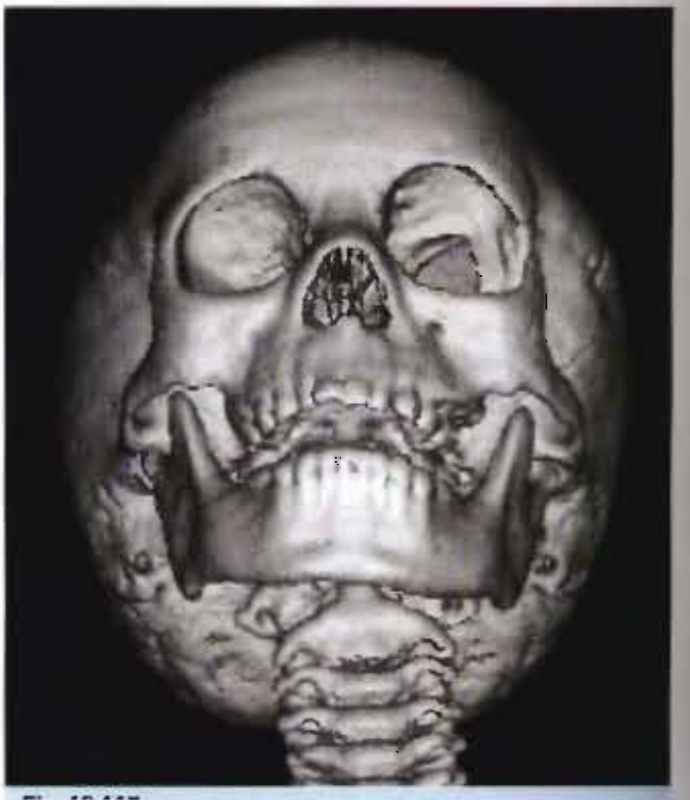


Fig. 18.117
Three-dimensional CT scan showing absence of the left greater wing of the sphenoid in NF-1 (Courtesy of D. Armstrong)

NF-1

NF-1 is the most common phakomatosis, affecting 1:4000 individuals, and it presents in childhood. The gene locus is on 17q11. The systemic features are discussed in Chapter 20. The ocular features are as follows:

1. **Orbital involvement** may be caused by one of the following:
   a. ***Optic nerve glioma*** (Fig. 18.116b and c) develops in about 15% of patients. It may be unilateral or bilateral and tends to extend posteriorly to involve the chiasm and hypothalamus (*see* Fig. 17.66).
   b. ***Other neural tumours*** including neurilemmoma, plexiform neurofibroma and meningioma.
   c. ***Spheno-orbital encephalocele*** is caused by absence of the greater wing of the sphenoid bone (Fig. 18.117). It characteristically causes a pulsating proptosis, unassociated with either a bruit or a thrill.
2. **Eyelid neurofibromas**, which may be either nodular (Fig. 18.118) or plexiform (Fig. 18.119), tend to develop early in life. When involving the upper lid, they frequently cause a mechanical ptosis.
3. **Iris lesions**
   a. ***Lisch nodules*** develop during the second to third decades and are eventually present in 95% of cases (*see* Fig. 18.116a).
   b. ***Congenital ectropion uveae*** is uncommon and may be associated with glaucoma (*see* Fig. 9.138).
   c. ***Mammillations*** are rare (*see* Fig. 4.81).
4. **Prominent corneal nerves** may occur (Fig. 18.120).
5. **Glaucoma** is relatively rare and, when present, is usually unilateral and congenital. About 50% of patients with glaucoma manifest ipsilateral neurofibroma of the upper eyelid and facial hemiatrophy. The mechanisms responsible for the pressure rise are discussed in Chapter 9.
6. **Fundus lesions**
   a. ***Choroidal naevi***, which may be multifocal and bilateral, are common. Patients with NF-1 and naevi are at increased risk for the subsequent development of choroidal melanoma.
   b. ***Retinal astrocytomas***, identical to those in tuberous sclerosis, are rare.

Fig. 18.118
Nodular neurofibroma

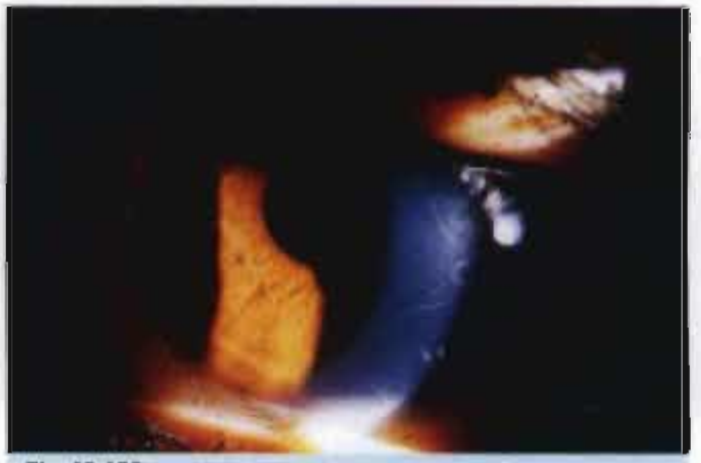


Fig. 18.120
Prominent corneal nerves

Fig. 18.119
Plexiform neurofibroma (Courtesy of K. Nischal)

NF-2

NF-2 is much less common than NF-1 and affects 1 in 40,000 individuals. The responsible gene locus is on 22q12. The main manifestations are bilateral acoustic neuromas and other CNS tumours (*see* Chapter 20). The following ocular lesions are often the first signs of the disease and may therefore assist in presymptomatic diagnosis:

1. **Cataract** affects about two-thirds of patients. The opacities develop prior to the age of 30 years and may be posterior subcapsular or capsular, cortical or mixed.
2. **Fundus lesions** consisting of combined hamartomas of the retinal pigment epithelium and retina and perifoveal epiretinal membranes are relatively common.
3. **Ocular motor defects** are present in about 10% of cases.
4. **Less common** findings include optic nerve sheath meningioma, optic nerve glioma, unilateral Lisch nodules, and an abnormal electroretinogram.

CHAPTER 19

Trauma

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Eyelid trauma

Haematoma

A haematoma (black eye) is the most common result of blunt injury to the eyelid or forehead and is generally innocuous. It is, however, very important to exclude the following more serious conditions:

1. **Trauma to the globe or orbit.** It is easier to examine the integrity of the globe before the lids become oedematous (Fig. 19.1).
2. **Orbital roof fracture,** if the black eye is associated with a subconjunctival haemorrhage without a visible posterior limit (Fig. 19.2).
3. **Basal skull fracture,** which may give rise to characteristic bilateral ring haematomas ('panda eyes') (Fig. 19.3).

Fig. 19.1
Severe periocular haematoma

Fig. 19.2
Periocular haematoma and subconjunctival haemorrhage

Fig. 19.3
'Panda eyes'

Laceration

The presence of a lid laceration, however insignificant, mandates careful exploration of the wound and examination of the globe. Any lid defect should be repaired by direct horizontal closure whenever possible, even if under tension, since this affords the best functional and cosmetic results (Thaller principle).

1. **Superficial** lacerations parallel to the lid margin without gaping can be sutured with 6-0 black silk. The sutures are removed after 5 days.
2. **Lid margin** lacerations invariably gape (Fig. 19.4a) and must therefore be very carefully sutured with perfect alignment to prevent notching.
   a. Evaluation for possible tissue loss.
   b. Conservative trimming of any irregular edges or grossly contaminated tissue (Fig. 19.4b).
   c. Initial eyelid margin realignment with a 6-0 black silk suture placed through the meibomian gland orifices. The bite should extend 2 mm on each side of the wound edge and be about 1 mm in depth (Fig. 19.5a).
   d. The tarsal plate is closed (Fig. 19.5b) using partial thickness long-acting absorbable sutures such as 6-0 polyglycolic acid (Dexon).

Fig. 19.4
Technique of suturing a marginal lid laceration (see text)
(Courtesy of Wilmer Institute)

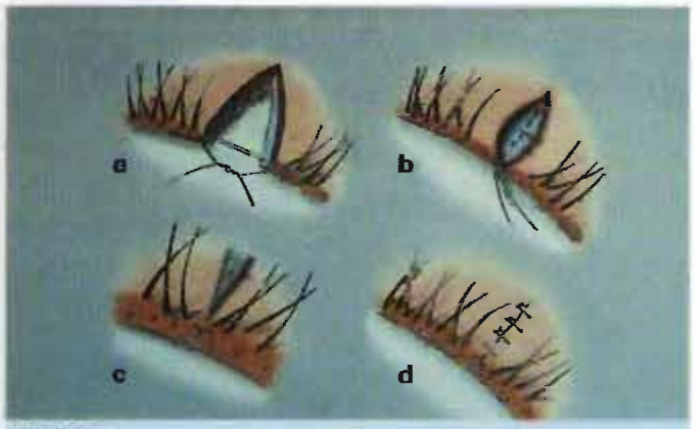

Fig. 19.5
Technique of suturing a marginal lid laceration (see text)
(Courtesy of Wilmer Institute)

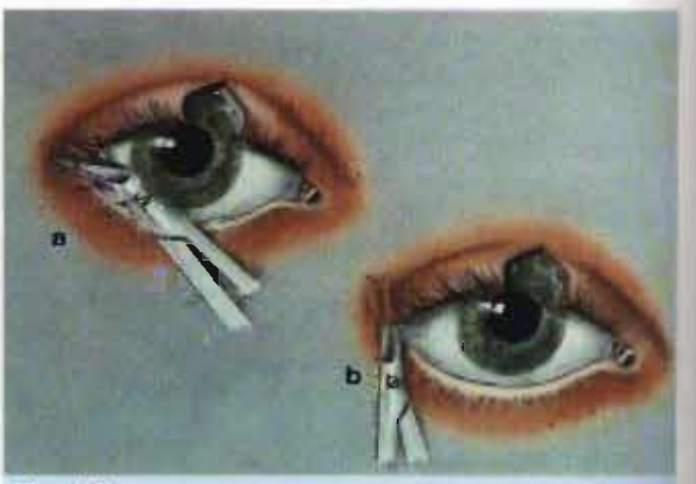

Fig. 19.7
Cantholysis (Courtesy of Wilmer Institute)

e. An additional lash line 6-0 silk suture is placed to achieve precise alignment of the tarsal margin and lashes (Fig. 19.5c).
f. The skin is closed with interrupted 6-0 black silk sutures (Fig. 19.5d).
g. The skin sutures are removed after 7–10 days.

Fig. 19.6
(a) Laceration of the lower lid; (b) after suturing

Fig. 19.8
Laceration involving the inferior canaliculus

Figure 19.6 shows the pre- and postoperative appearances.

3. **Lacerations with tissue loss** just sufficient to prevent direct primary closure can usually be managed by performing a lateral cantholysis (Fig. 19.7) in order to increase lateral eyelid mobility.
4. **Lacerations with extensive tissue loss** may require major reconstructive procedures such as used following lid resection for malignant tumours (*see* Chapter 1).
5. **Canalicular lacerations** (Fig. 19.8) should be repaired within 24 hours.
   a. The laceration is bridged by silicone tubing, which is threaded down the lacrimal system and tied in the nose (Figs 19.9, 19.10 and 19.11 illustrate the principles of lacrimal intubation).
   b. The laceration is sutured.
   c. The tubing is left in situ for 3–6 months.

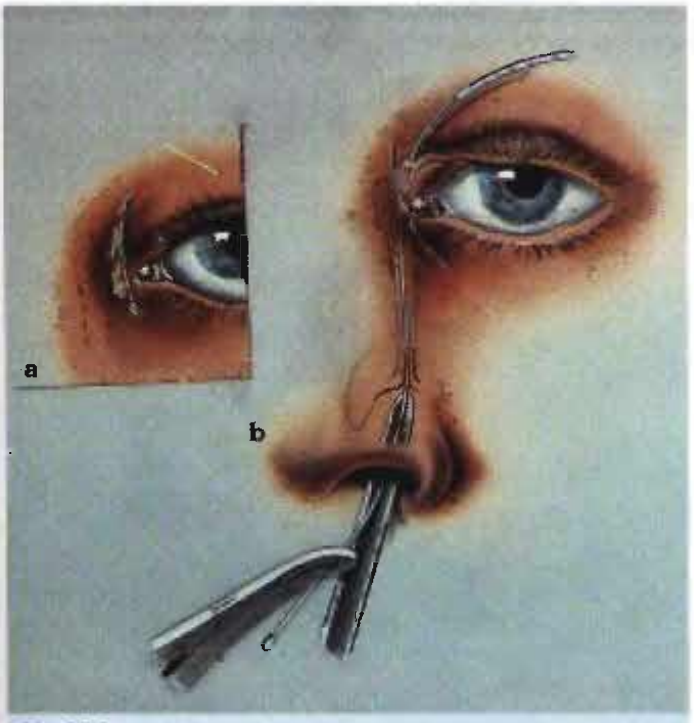

Fig. 19.9
Intubation of the lacrimal system (see *text*) (Courtesy of Wilmer Institute)

Fig. 19.10
Intubation of the lacrimal system (see *text*) (Courtesy of Wilmer Institute)

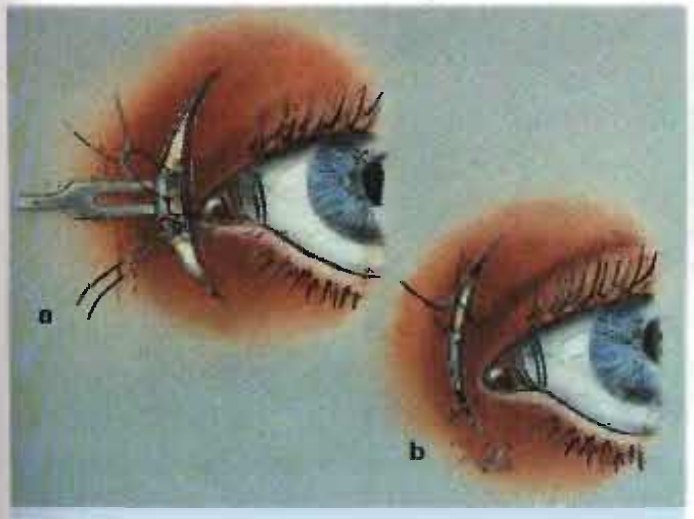

Fig. 19.11
Intubation of the lacrimal system (see *text*) (Courtesy of Wilmer Institute)

Fig. 19.12
Mechanism of an orbital floor blow-out fracture

Orbital fractures

Blow-out orbital floor fracture

A 'pure' blow-out fracture of the orbit does not involve the orbital rim whereas an 'impure' fracture involves the orbital rim and adjacent facial bones. A blow-out fracture of the orbital floor is typically caused by a sudden increase in the orbital pressure by a striking object which is greater than 5 cm in diameter, such as a fist or tennis ball (Fig. 19.12). Since the bones of the lateral wall and the roof are usually able to withstand such trauma, the fracture most frequently involves the floor of the orbit along the thin bone covering the infraorbital canal. Occasionally, the medial orbital wall may also be fractured. Clinical features vary with the severity of trauma and the time interval between injury and examination.

Signs

1. **Periocular signs** include variable ecchymosis, oedema and subcutaneous emphysema (Fig. 19.13a).
2. **Infraorbital nerve anaesthesia** involving the lower lid, cheek, side of nose, upper lip, upper teeth and gums is very common because a blow-out fracture frequently involves the infraorbital canal.
3. **Diplopia** may be caused by one of the following mechanisms:
   - Haemorrhage and oedema of the orbit may cause the septa, which connect the inferior rectus and inferior oblique muscles to the periorbita, to become taut and thus restrict movements of the globe. Ocular motility usually improves as haemorrhage and oedema resolve.
   - Mechanical entrapment within the fracture of the inferior rectus or inferior oblique muscle, or adjacent connective tissue and fat. Diplopia typically occurs in both upgaze (Fig. 19.13b) and downgaze (double diplopia). In these cases the forced duction test and the differential intraocular pressure tests are positive. Diplopia may subsequently improve if mainly due to entrapment of connective tissue and fat, but usually persists if there is significant involvement of the muscles themselves.
   - Direct injury to an extraocular muscle is associated with a negative forced duction test. The muscle fibres usually regenerate and normal function returns within about 2 months.
4. **Enophthalmos** (Fig. 19.13c) may be present if the fracture is severe, although it tends to manifest after a few days, as the initial oedema resolves. In the absence of surgical intervention, enophthalmos may continue to increase for about 6 months as post-traumatic orbital degeneration and fibrosis develop.
5. **Ocular damage** (e.g. hyphaema, angle recession, retinal dialysis), although uncommon, should be excluded by careful slit-lamp and fundus examination.

Investigations

1. **CT** with coronal sections (Fig. 19.14) is particularly useful in evaluating the extent of the fracture, as well as determining the nature of maxillary antral soft-tissue densities which may represent prolapsed orbital fat, extraocular muscles, haematoma or unrelated antral polyps.
2. **Hess test** (Fig. 19.15) is useful in assessing and monitoring the progression of diplopia.
3. **Field of binocular vision** can be assessed on the Lister or Goldmann perimeter.

Fig. 19.13
Right orbital floor blow-out fracture. (a) Mild bruising, superficial laceration and dilated pupil following fundus examination; (b) restricted elevation; (c) mild enophthalmos

Fig. 19.14
Coronal CT scan of a right orbital floor blow-out fracture showing the 'tear drop' sign

Treatment

1. **Initial treatment** is conservative with antibiotics if the fracture involves the maxillary sinus. The patient should also be instructed not to blow the nose.
2. **Subsequent treatment** is aimed at prevention of permanent vertical diplopia and/or cosmetically unacceptable enophthalmos. The three factors that determine the risk of these late complications are fracture size, herniation of orbital contents into the maxillary sinus and muscle entrapment. Although there may be some overlap, most fractures fall into one of the following categories:
   - Small cracks unassociated with herniation do not require treatment as the risk of permanent complications is small.
   - Fractures involving less than half the orbital floor, with little or no herniation, and improving diplopia also do not require treatment unless more than 2 mm of enophthalmos develops.
   - Fractures involving half or more of the orbital floor with entrapment of orbital contents and persistent diplopia in the primary position should be repaired within 2 weeks. If surgery is delayed, the results are less satisfactory because secondary fibrotic changes develop in the orbit.
3. **Technique of surgical repair**
   a. A transconjunctival or subciliary incision is made (Fig. 19.16a).
   b. The periosteum is elevated from the floor of the orbit and all entrapped orbital contents are removed from the antrum (Fig. 19.16b).
   c. The defect in the floor is repaired by using synthetic material such as Supramid, silicone or Teflon (Fig. 19.16c).

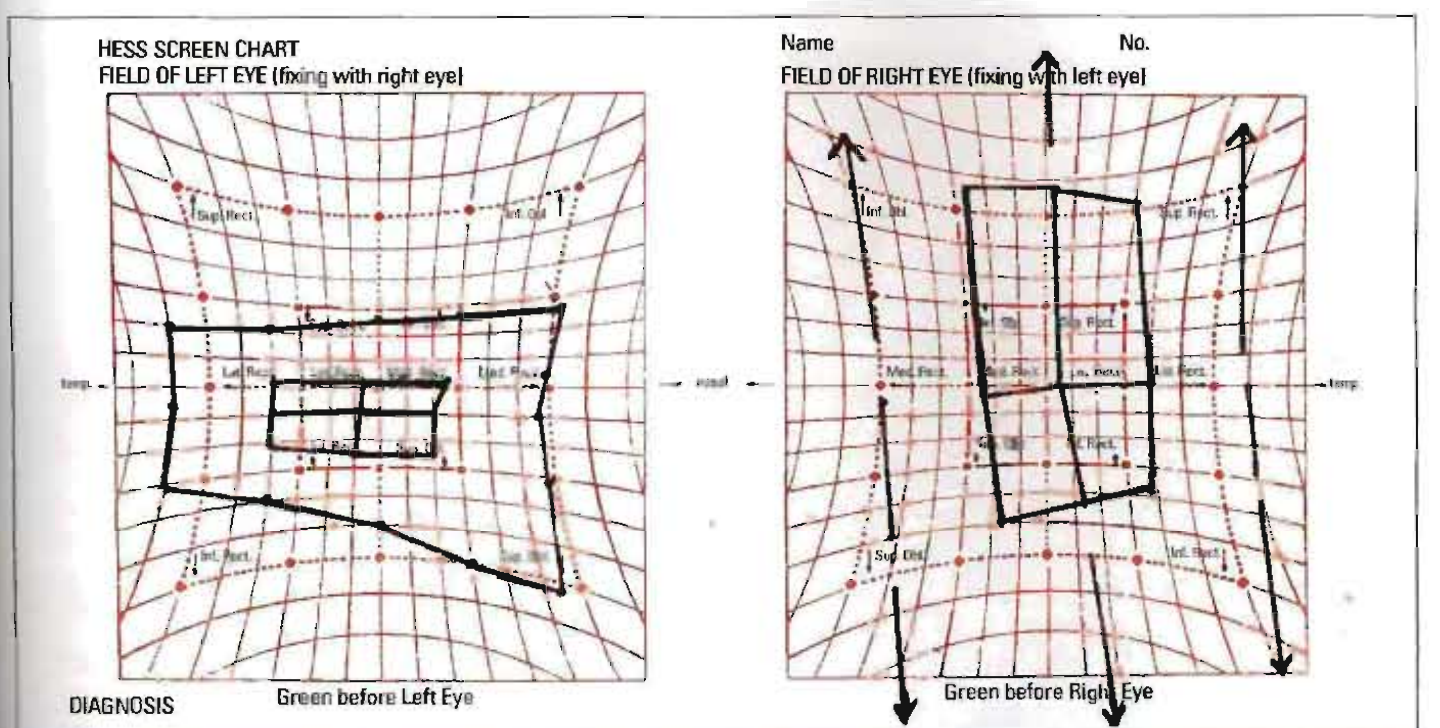

Fig. 19.15
Hess chart of a left orbital floor blow-out fracture showing restriction of left upgaze (superior rectus and inferior oblique) and restriction on downgaze (inferior rectus). There is also considerable secondary overaction of the right eye

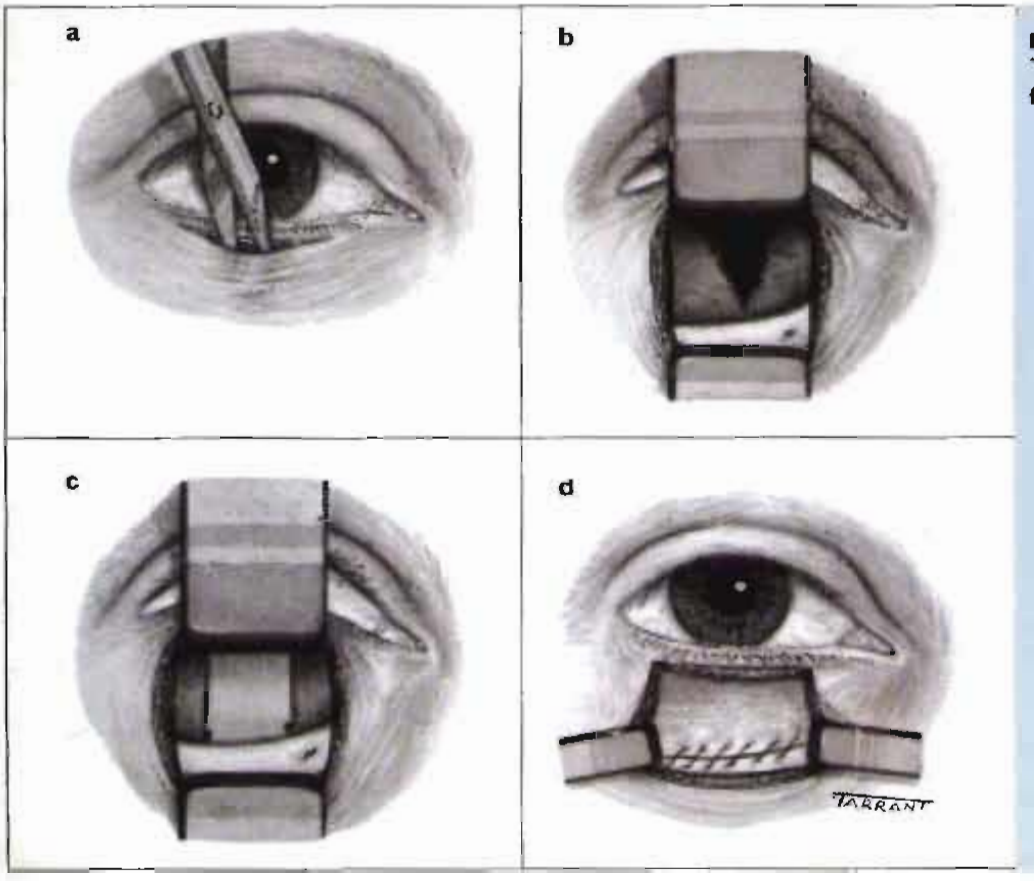

Fig. 19.16
Technique of repair of an orbital floor blow-out fracture (see text)

Fig. 19.17
Coronal CT scan following repair of a right orbital floor blow-out fracture with synthetic material

d. The periosteum is sutured (Fig. 19.16d).

Figure 19.17 is a coronal CT scan showing the post-operative appearance following repair of a right blow-out fracture with a plastic implant.

Blow-out medial wall fracture

Most medial wall orbital fractures are associated with floor fractures (Fig. 19.18). Isolated fractures are less common.

1. **Signs**
   - Periorbital subcutaneous emphysema (Fig. 19.19), which typically develops when the patient blows the nose. Because of the possibility of forcing infected sinus contents into the orbit, blowing of the nose should be discouraged.
   - Defective ocular motility involving adduction and abduction (Fig. 19.20), if the medial rectus muscle is entrapped in the fracture.
2. **Treatment** involves release of the entrapped tissue and repair of the bony defect.

Roof fracture

Roof fractures are rarely encountered by ophthalmologists. Isolated fractures, caused by minor trauma such as falling on a sharp object or a blow to the brow or forehead, are most common in young children. Complicated fractures, caused by major trauma with associated displacement of the orbital rim

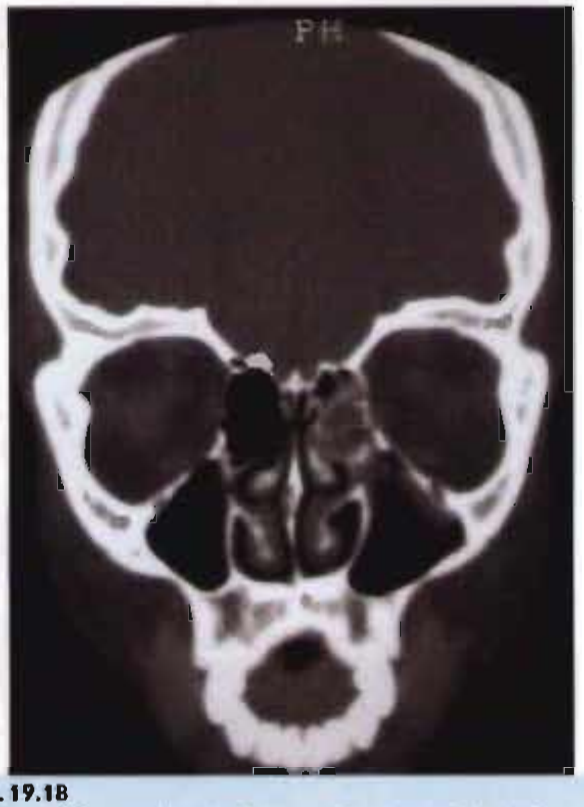

Fig. 19.18
Coronal CT scan showing blow-out fractures of the left medial orbital wall and floor

Fig. 19.19
Subcutaneous emphysema in a patient with a medial orbital wall blow-out fracture

or significant disturbance of other craniofacial bones, most commonly affect adults.

1. **Presentation** is with a haematoma of the upper eyelid and periocular ecchymosis which develop after a few hours and may later spread to the opposite side (*see* Fig. 19.3).
2. **Signs**
   - Inferior or axial displacement of the globe.
   - Large fractures may be associated with pulsation of the globe unassociated with a bruit, due to transmission of CSF pulsation, best detected on applanation tonometry, if possible.

Fig. 19.20
Limitation of left abduction due to entrapment of the left medial rectus muscle in a medial orbital wall blow-out fracture

3. **Treatment**
   - Small fractures may not require treatment but it is important to observe the patient for the possibility of a CSF leak which may lead to meningitis.
   - Sizeable bony defects with downwardly displaced fragments usually require reconstructive surgery.

Lateral wall fracture

Acute lateral wall fractures (Fig. 19.21) are rarely encountered by ophthalmologists. Because the lateral wall of the orbit is more solid than the other walls, a fracture is usually associated with extensive facial damage.

Fig. 19.21
Axial CT scan showing a right lateral wall fracture with bony fragments impinging on the optic nerve

Trauma to the globe

Introduction

Definitions

1. **Closed injury** is commonly due to blunt trauma. The corneoscleral wall of the globe is intact; however, intraocular damage may be present.

2. **Open injury** involves a full-thickness wound of the corneoscleral wall.
3. **A contusion** is a closed injury resulting from blunt trauma. Damage may occur at the site of impact or at a distant site.
4. **A rupture** is a full-thickness wound, caused by blunt trauma. The globe gives way at its weakest point, which may not be at the site of impact.
5. **A laceration** is a full-thickness wound caused by a sharp object at the site of impact.
6. **A lamellar laceration** is a partial-thickness wound caused by a sharp object.
7. **Penetration** is a single full-thickness wound, usually caused by a sharp object, without an exit wound. Such a wound may be associated with intraocular retention of a foreign body.
8. **Perforation** consists of two full-thickness wounds, one entry and one exit, usually caused by a missile.

General principles of management

1. **Initial assessment** should be performed in the following order:
   - Determination of the nature and extent of any life-threatening problems.
   - History of the injury, including the circumstances, timing and likely object.
   - Thorough examination of both eyes and orbits.
2. **Special investigations**
   a. Plain radiographs may be taken when a foreign body is suspected (Fig. 19.22).
   b. CT is superior to plain radiography in the detection and localization of intraocular foreign bodies (Fig. 19.23). It is also of value in determining the integrity of intracranial, facial and intraocular structures.

> *NB:* MRI should never be performed if a metallic foreign body is suspected.

c. Ultrasonography may be useful in the detection of intraocular foreign bodies (Fig. 19.24), globe rupture, suprachoroidal haemorrhage and retinal detachment. It is also helpful in planning surgical repair, for example regarding placement of infusion ports during vitrectomy and whether drainage of suprachoroidal haemorrhage is required.

d. Electrophysiological tests may be useful in assessing the integrity of the optic nerve and retina, particularly if some time has passed since the original injury and there is suspicion of a retained intraocular foreign body.

Fig. 19.22
Plain radiograph showing a left airgun pellet

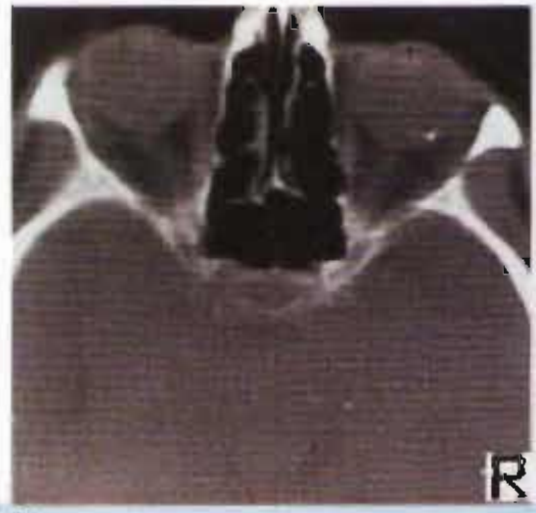

Fig. 19.23
Axial CT scan showing a left intraocular foreign body (Courtesy of Wilmer Institute)

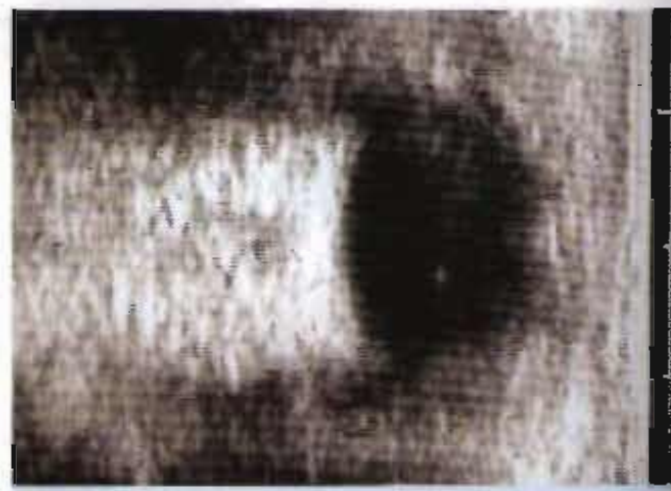

Fig. 19.24
B-scan ultrasonograph showing an intraocular foreign body

Blunt trauma

The most common causes of blunt trauma are squash balls, elastic luggage straps and champagne corks. Severe blunt trauma results in anteroposterior compression with simultaneous expansion in the equatorial plane (Fig. 19.25), associated with a transient but severe increase in intraocular pressure. Although the impact is primarily absorbed by the lens–iris diaphragm and the

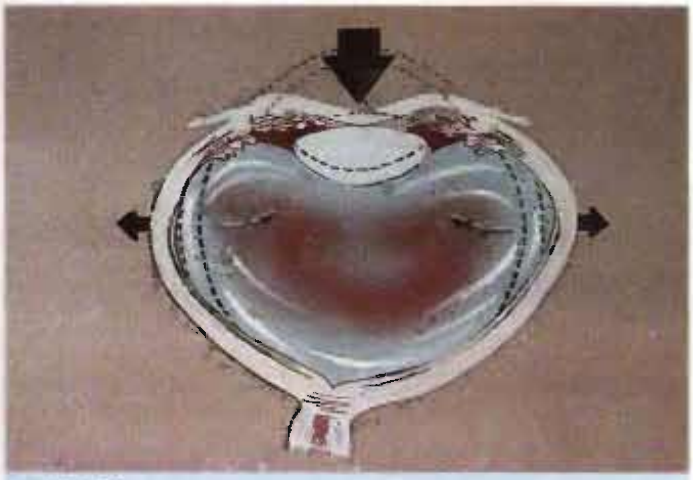

Fig. 19.25
Mechanism of ocular damage by blunt trauma (Courtesy of Wilmer Institute)

vitreous base, damage can also occur at a distant site such as the posterior pole. The extent of ocular damage depends on the severity of trauma and for unknown reasons, is largely concentrated to either anterior or posterior segment. Apart from obvious ocular damage, blunt trauma commonly results in long-term effects: the prognosis is therefore necessarily guarded.

Anterior segment complications

1. **A corneal abrasion** involves a breach of the epithelium, which stains with fluorescein. If over the pupillary area, vision may be grossly impaired. This exquisitely painful condition is commonly treated with topical cycloplegia to promote comfort and antibiotic ointment. Although patching has been standard treatment in the past it has become apparent that the cornea heals faster with less pain when not patched.
2. **Acute corneal oedema** may develop, secondary to focal or diffuse dysfunction of the corneal endothelium. It is commonly associated with folds in Descemet membrane and stromal thickening, which clear spontaneously.
3. **Hyphaema** (haemorrhage into the anterior chamber) is a common complication. The source of the bleeding is the iris or ciliary body. Characteristically, the red blood cells sediment inferiorly with a resultant 'fluid' level, the height of which should be measured and documented (Fig. 19.26). Most traumatic hyphaemas are innocuous and transient and merely require daily observation until they resolve spontaneously. The immediate risk is that of secondary haemorrhage, often larger than the original hyphaema, which may occur at any time up to a week after the original injury (most commonly within the first 24 hours). The main aims of treatment are therefore prevention of secondary haemorrhage, control of any elevation of intraocular pressure and management of associated complications. Oral tranexamic acid 25 mg/kg t.i.d., an antifibrolytic agent, is useful for the former. Opinions vary, but it would appear sensible to immobilize the pupil in the dilated state, with atropine to prevent further haemorrhage. Hospital admission for a few days may be advisable so that intraocular pressure may be monitored and, if elevated, treated appropriately so as to prevent secondary corneal blood-staining (*see* Chapter 9). Traumatic uveitis is treated with topical steroids and mydriatics.
4. **The anterior uvea** may manifest structural and/or functional damage.
   a. ***Pupil.*** Severe contusion is often accompanied by transient miosis evidenced by the pattern of pigment imprinting on the anterior lens capsule (Vossius ring), which corresponds to the size of the miosed pupil (*see* Fig. 8.19). Alternatively, damage to the iris sphincter may result in traumatic mydriasis, which is often permanent: the pupil reacts sluggishly or not at all to both light and accommodation. Radial tears in the pupillary margin are common (Fig. 19.27).
   b. ***Iridodialysis*** is a dehiscence of the iris from the ciliary body at its root. The pupil is typically 'D' shaped and the dialysis is seen as a dark biconvex area near the limbus (Fig. 19.28). An iridodialysis may be asymptomatic if

Fig. 19.26
Traumatic hyphaema

Fig. 19.27
Rupture of the iris sphincter

Fig. 19.28
Inferior iridodialysis

Fig. 19.29
Traumatic aniridia (Courtesy of Wilmer Institute)

covered by the upper lid; if exposed in the palpebral aperture, uniocular diplopia and glare may ensue, sometimes necessitating surgical repair of the dehiscence. Traumatic aniridia (360° iridodialysis) may rarely occur (Fig. 19.29).

c. ***The ciliary body*** may react to severe blunt trauma by temporary cessation of aqueous secretion (ciliary shock) resulting in ocular hypotony. Tears extending into the face of the ciliary body (angle recession) (Fig. 19.30) are associated with a risk of late glaucoma (*see* Chapter 9).

5. Lens

a. ***Cataract*** formation is a common sequel to blunt trauma. Postulated mechanisms include traumatic damage to the lens fibres themselves and minute ruptures in the lens capsule with influx of aqueous humour, hydration of lens fibres and consequent opacification. A ring-shaped faint anterior subcapsular opacity may underly Vossius ring. Commonly opacification occurs in the posterior subcapsular cortex along the posterior sutures ('rosette-shaped' cataract) (*see* Fig. 8.20) which may subsequently disappear, remain stationary or progress to maturity. Cataract surgery may be necessary for visually significant opacity.

Fig. 19.30
Severe angle recession

b. ***Subluxation*** of the lens may occur, secondary to tearing of the suspensory ligament. A subluxated lens tends to deviate towards the meridian of intact zonule; the anterior chamber may deepen over the area of zonular dehiscence, if the lens rotates posteriorly. The edge of a subluxated lens may be visible under mydriasis and the iris may tremble on ocular movement (iridodonesis). Subluxation of magnitude sufficient to render the pupil partly aphakic may result in uniocular diplopia; additional lenticular astigmatism due to lens tilt may occur.

c. ***Dislocation*** due to 360° rupture of the zonule is rare and may be into the vitreous, or less commonly into the anterior chamber (Fig. 19.31).

6. Rupture of the globe may result from very severe blunt trauma. The rupture is usually anterior, in the vicinity of Schlemm canal, with prolapse of intraocular structures such as lens, iris, ciliary body and vitreous (Fig. 19.32). Occasionally, the rupture is posterior (occult) with little visible damage to the anterior segment. Clinically, occult rupture should be suspected if there is asymmetry of anterior chamber depth and intraocular pressure in the

Fig. 19.31
Lens dislocation into the anterior chamber

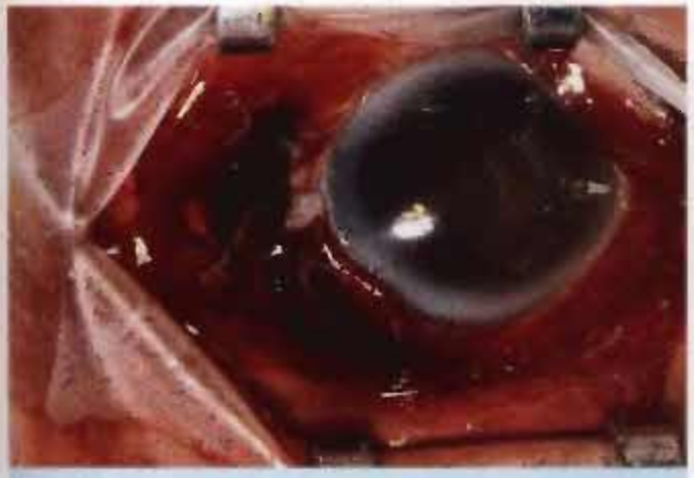

Fig. 19.32
Rupture of the globe (Courtesy of Wilmer Institute)

affected eye is low. The principles of repairing scleral ruptures are described later.

Posterior segment complications

1. **Posterior vitreous detachment**, which may be associated with vitreous haemorrhage, may be seen. Pigment cells similar to tobacco dust may be seen floating in the anterior vitreous.
2. **Commotio retinae** indicates concussion of the sensory retina resulting in cloudy swelling which gives the involved area a grey appearance. Commotio most frequently involves the temporal fundus (Fig. 19.33) and occasionally the macula, when a 'cherry red spot' may be seen at the fovea (Fig. 19.34). The prognosis in mild cases is good with spontaneous resolution without sequelae within 6 weeks. Severe involvement of the macula may be associated with intraretinal haemorrhage. Subsequent post-traumatic macular changes include progressive pigmentary degeneration and macular hole formation.
3. **Choroidal rupture** involves the choroid, Bruch membrane and RPE; it may be direct or indirect. Direct ruptures

Fig. 19.33
Peripheral commotio retinae

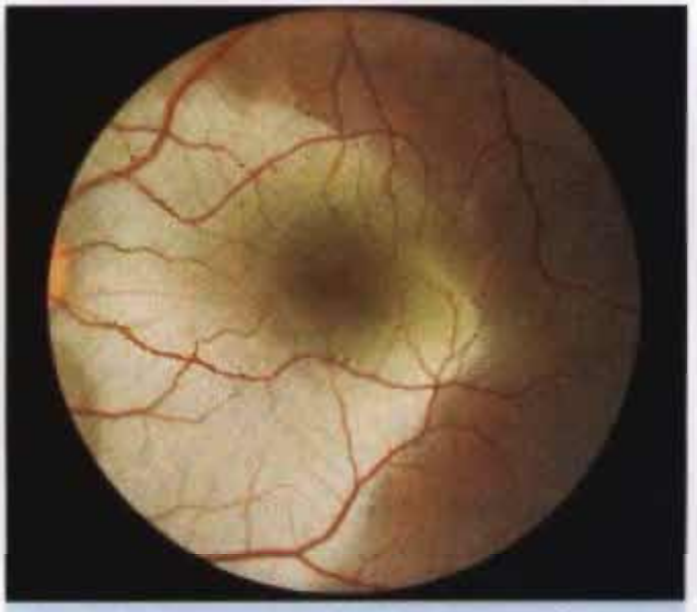

Fig. 19.34
Commotio retinae involving the macula

Fig. 19.35
Acute choroidal rupture with subretinal haemorrhage

are located anteriorly at the site of impact and run parallel with the ora serrata. Indirect ruptures occur opposite the site of impact. A fresh rupture may be partially obscured by subretinal haemorrhage (Fig. 19.35), which may break through the internal limiting membrane with resultant subhyaloid or vitreous haemorrhage. Weeks to months later, on absorption of the blood, a white crescent-shaped, vertical streak of exposed underlying sclera, frequently involving the macula, concentric with the optic disc becomes visible (Fig. 19.36). The visual prognosis is poor if the fovea is involved. An uncommon late complication is secondary choroidal neovascularization which may result in haemorrhage, scarring and further visual deterioration.

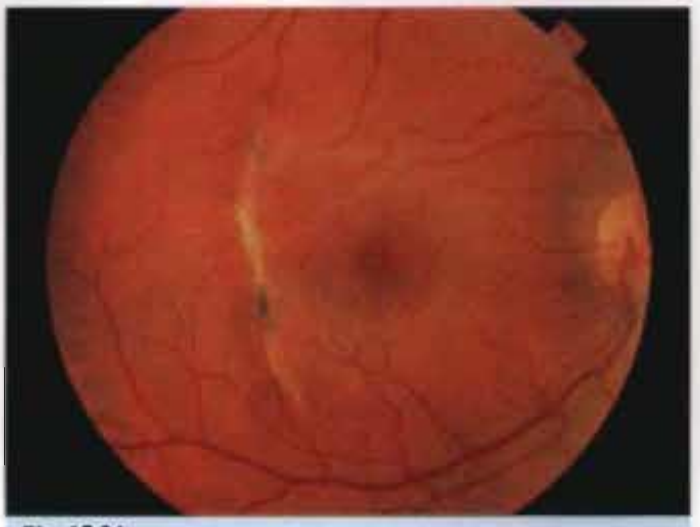

Fig. 19.36
Old choroidal rupture

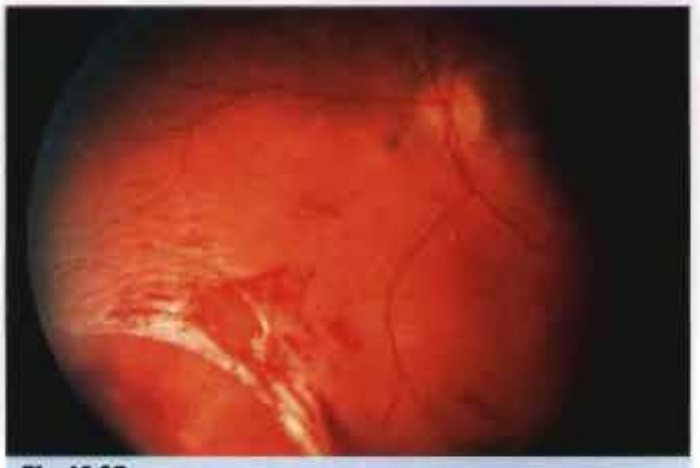

Fig. 19.37
Traumatic retinal dialysis (Courtesy of Wilmer Institute)

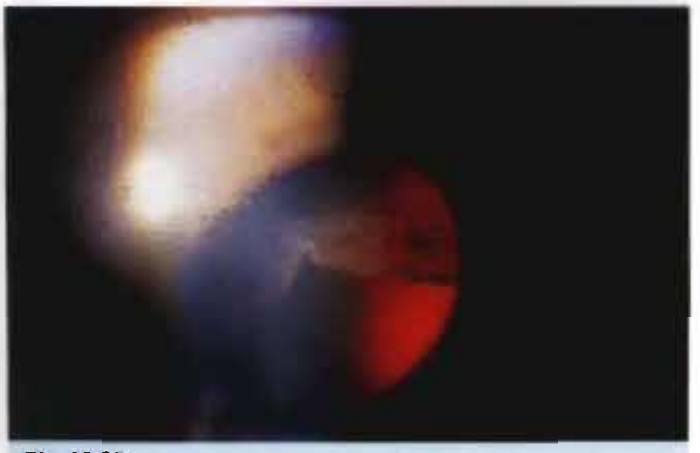

Fig. 19.38
Avulsion of the vitreous base

aspect of the vitreous base. The vitreous base may become avulsed, giving rise to a 'bucket-handle' appearance which comprises a strip of ciliary epithelium, ora serrata and the immediate post-oral retina into which basal vitreous gel remains inserted (Fig. 19.38). Traumatic dialyses may occur in any quadrant but are most frequent in the upper nasal, perhaps because trauma is frequently from an inferotemporal direction. Although they occur at the time of injury, any subsequent retinal detachment usually does not develop until several months later. Progression is slow, probably because the vitreous gel is healthy.

   b. ***Equatorial tears*** are less frequent and due to direct retinal disruption at the point of scleral impact. They may occasionally extend for more than one quadrant (giant tears).
   c. ***Macular holes*** may occur either at the time of injury or later following the resolution of commotio retinae.

4. **Retinal breaks**, which may lead to retinal detachment, are of three main types:
   a. ***Retinal dialyses*** (Fig. 19.37) are caused by traction by the relatively inelastic vitreous gel along the posterior

5. **Optic nerve**
   a. ***Optic neuropathy*** is an uncommon but often devastating cause of permanent visual loss following contusive injuries to the head, particularly the forehead. This impact is thought to transmit a shock wave to the optic canal, damaging the optic nerve. Typically the optic nerve head and fundus are initially normal, the only objective finding being a relative afferent pupillary defect. Neither systemic steroids nor surgical decompression of the optic canal prevent the development of optic atrophy within 3–4 weeks.
   b. ***Optic nerve avulsion*** is rare and typically occurs when an object intrudes between the globe and the orbital wall, displacing the eye. Postulated mechanisms include sudden extreme rotation or anterior displacement of the globe. Avulsion may be isolated or occur in

Fig. 19.39
Avulsed optic nerve (Courtesy of E.M. Eagling, M.J. Roper-Hall, Eye Injuries, Butterworths, 1986)

association with other injuries to the globe or orbit. Fundus examination shows a striking cavity where the optic nerve head has retracted from its dural sheath (Fig. 19.39). There is no treatment; the visual prognosis depends on whether avulsion is partial or complete.

Non-accidental injury

Non-accidental injury (shaken baby syndrome) indicates physical abuse in children usually under the age of 2 years, and should be suspected whenever characteristic ophthalmic features are identified in the absence of a convincing alternative explanation. The diagnosis should be considered with the help of a specialist paediatrician; most hospitals dealing with children will have a child abuse team. The injury may be caused by violent shaking alone. However, careful examination also frequently reveals signs of impact injuries. Brain damage is thought to be the result of hypoxia and ischaemia resulting from apnoea, rather than shearing or impact.

1. **Presentation** is frequently with irritability, lethargy and vomiting, which may be initially misdiagnosed as gastroenteritis or other infection because the history of injury is withheld.
2. **Systemic features** include subdural haematoma and impact injuries to the head, ranging from skull fractures to soft tissue bruises. Many survivors suffer significant permanent neurological handicap.
3. **Ocular features** are many and varied. The most important are as follows:
   - Retinal haemorrhages, unilateral or bilateral, are the most common feature. The haemorrhages typically involve different layers of the retina and are most obvious in the posterior pole (Fig. 19.40), although they often extend to the periphery.
   - Periocular bruising and subconjunctival haemorrhages.
   - Poor visual responses and afferent pupillary defects.
   - Visual loss occurs in about 20% of cases largely as a result of cerebral damage.

Fig. 19.40
Haemorrhages in non-accidental injury

Penetrating trauma

Causes

Penetrating injuries are three times more common in males than females, and in the younger age group. The most frequent causes are assault, domestic accidents and sport. The extent of the injury is determined by the size of the object, its speed at the time of impact and its composition. Sharp objects such as knives cause well-defined lacerations of the globe. However, the extent of damage caused by flying foreign bodies is determined by their kinetic energy. For example, an airgun pellet is large and, although relatively slow moving, has a high kinetic energy and can thus cause considerable ocular damage. In contrast, a fast-moving fragment of shrapnel has a low mass and therefore will cause a well-defined laceration with relatively less intraocular damage than an airgun pellet.

> ***NB:*** Of paramount immediate importance is the introduction of infection with any penetrating injury. Endophthalmitis or panophthalmitis, often more severe than the initial injury, may ensue with loss of the eye.

Tractional retinal detachment

Tractional retinal detachment may occur secondary to vitreous incarceration in the wound and intragel vitreous haemorrhage (Fig. 19.41a), which stimulates fibroblastic proliferation along the planes of incarcerated vitreous (Fig. 19.42). Subsequent contraction of such membranes leads to shortening and a rolling effect on the peripheral retina in the region of the vitreous base and eventually to tractional retinal detachment (*see* Fig. 19.41b).

Principles of primary repair

The technique of primary repair depends on the severity of the wound and any associated complications such as iris

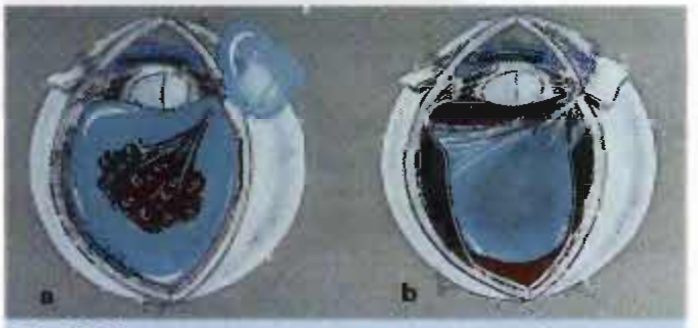

Fig. 19.41
(a) Penetrating injury resulting in vitreous prolapse and intraocular haemorrhage; (b) subsequent proliferation and vitreoretinal traction resulting in retinal detachment (Courtesy of Wilmer Institute)

Fig. 19.42
Retrolental fibrous proliferation following penetrating trauma

Fig. 19.45
Penetrating corneal wound with a flat anterior chamber

Fig. 19.43
Penetrating corneal wound with a formed anterior chamber (Courtesy of Wilmer Institute)

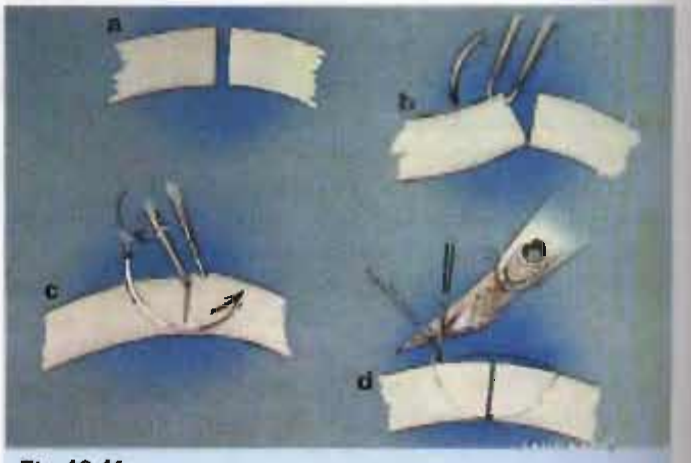

Fig. 19.46
Technique of repair of a penetrating corneal wound. The anterior chamber may be deepened with a viscoelastic substance (Courtesy of Wilmer Institute)

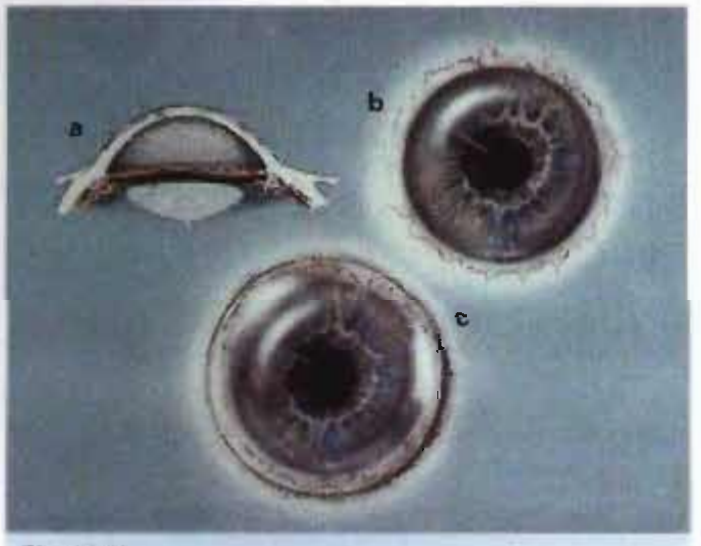

Fig. 19.44
(a and b) Penetrating corneal wound with a formed anterior chamber; (c) bandage contact lens in situ (Courtesy of Wilmer Institute)

incarceration, flat anterior chamber and damage to intraocular contents.

1. **Small shelving corneal lacerations** (Figs 19.43 and 19.44a and b) with formed anterior chamber may not require suturing as they often heal spontaneously or with the aid of a soft bandage contact lens (Fig. 19.44c).
2. **Medium-sized corneal lacerations** usually require suturing, especially if the anterior chamber is shallow or flat (Fig. 19.45). The technique of suturing is shown in Figs 19.46 and 19.47. If the laceration involves the limbus it is important to expose the adjacent sclera (Fig. 19.48) and to suture any scleral extension (Fig. 19.49). A shallow anterior chamber may re-form spontaneously once the cornea has been sutured, if not it should be reformed with balanced salt solution. A postoperative bandage contact lens may also be useful for a few days to ensure that the anterior chamber remains deep.
3. **Corneal lacerations with iris involvement** (Fig. 19.50 and 19.51a). Management depends on the duration and extent of incarceration.

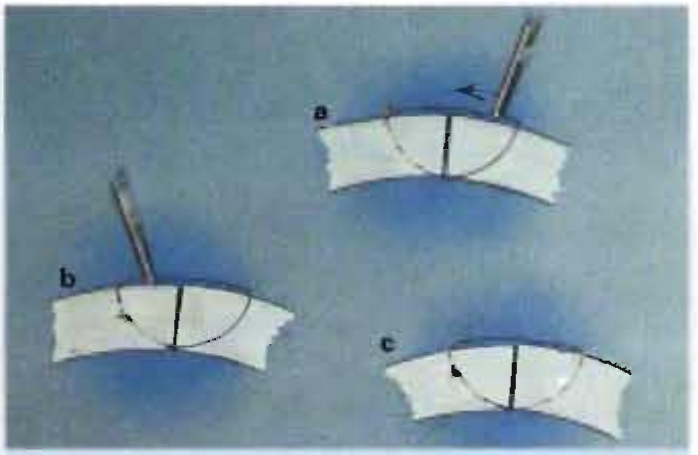

Fig. 19.47
Technique of burying the knot (Courtesy of Wilmer Institute)

Fig. 19.50
Penetrating corneal wound with iris prolapse (Courtesy of Wilmer Institute)

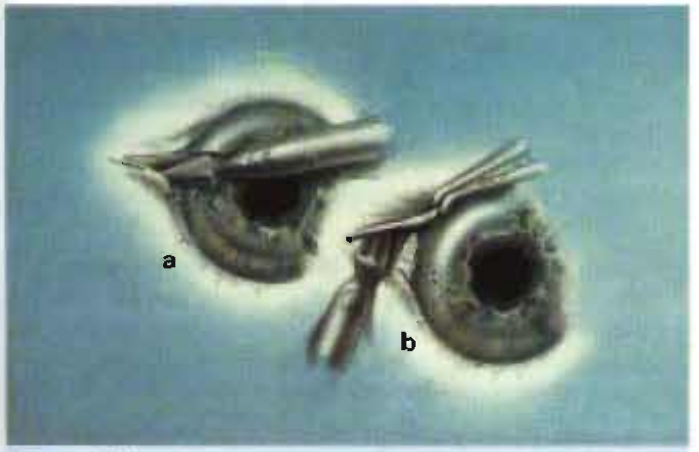

Fig. 19.48
Exploration of the sclera following repair of a corneal laceration (Courtesy of Wilmer Institute)

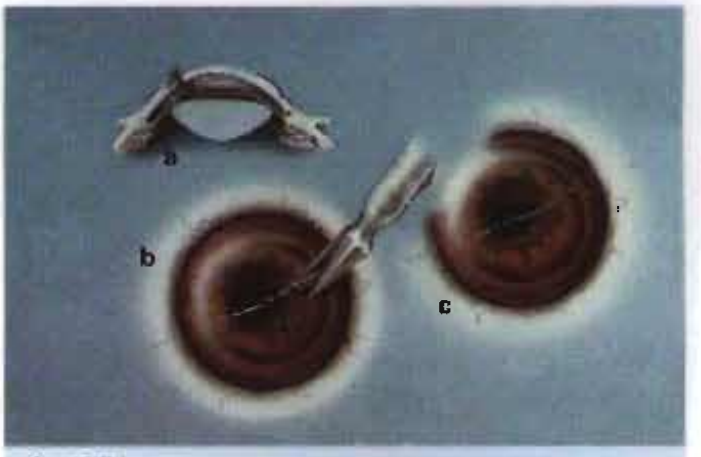

Fig. 19.51
(a) Penetrating corneal wound with iris prolapse; (b) abscision of prolapsed iris; (c) final appearance

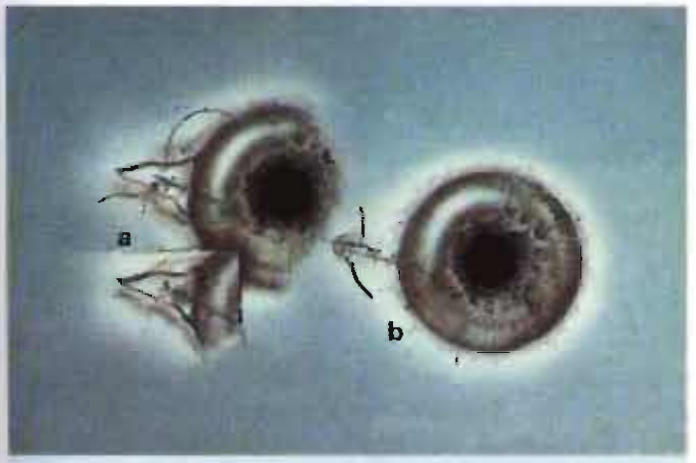

Fig. 19.49
Repair of a scleral laceration (Courtesy of Wilmer Institute)

Fig. 19.52
Corneal laceration associated with cataract

- A small peak of recently incarcerated iris may be reposited and the pupil constricted with intracameral acetylcholine.
- Large incarcerations of iris should be abscised (Fig. 19.51b), especially if of more than a few days' duration or the iris appears non-viable, due to the risk of endophthalmitis.

4. **Corneal laceration with lenticular damage** (Figs 19.52 and 19.53a) is treated by suturing the laceration and

Fig. 19.53
(a) Penetrating wound with disruption of the lens and anterior herniation of vitreous through a ruptured zonule; (b) repair of corneal wound followed by lensectomy and anterior vitrectomy (Courtesy of Wilmer Institute)

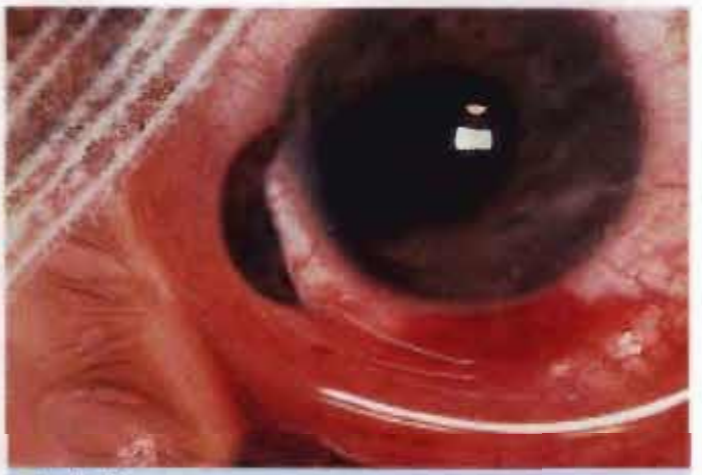

Fig. 19.54
Scleral laceration with iridociliary prolapse (Courtesy of Wilmer Institute)

removing the lens by phacoemulsification or with a vitreous cutter (Fig. 19.53b). The latter is preferred if there is associated vitreous involvement. Primary implantation of an intraocular lens is frequently associated with a favourable visual outcome and a low rate of postoperative complications.

5. **Anterior scleral lacerations** limited to the insertions of the recti (i.e. anterior to the spiral of Tillaux and therefore the ora serrata) have a better prognosis than more posterior wounds. An anterior scleral wound may, nevertheless, be associated with serious complications such as iridociliary prolapse and vitreous incarceration (Fig. 19.54). The latter, unless appropriately managed, may result in subsequent vitreoretinal traction and retinal detachment. Every attempt should be made to reposit exposed viable uveal tissue and cut prolapsed vitreous flush with the wound.

NB: Cellulose sponges should not be used to remove vitreous for fear of inducing vitreous traction.

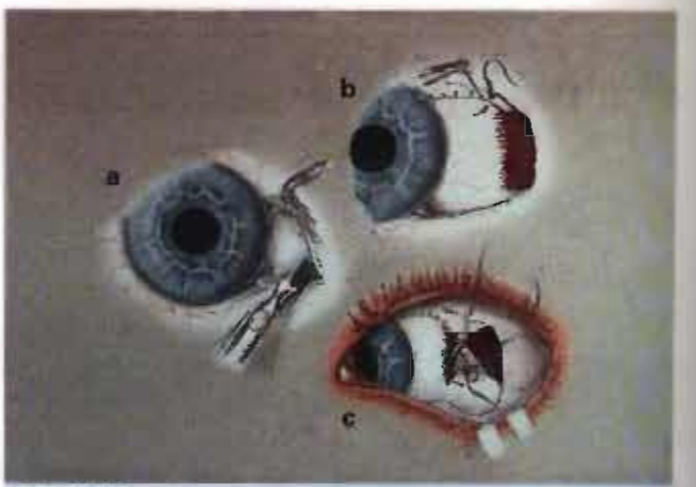

Fig. 19.55
(a) Exposure of sclera; (b and c) repair of scleral laceration (Courtesy of Wilmer Institute)

6. **Posterior scleral lacerations** are frequently associated with retinal breaks unless very superficial. The scleral wound is exposed (Fig. 19.55a) and sutured starting anteriorly and working posteriorly (Fig. 19.55b and c). It may also be necessary to treat retinal breaks prophylactically.

NB: During repair it is very important not to exert excessive pressure and traction on the eye to prevent or minimize loss of intraocular contents.

Aims of secondary repair

Secondary repair of posterior segment trauma, if appropriate, is usually carried out 10–14 days after primary repair. This allows time not only for healing of wounds but also for the development of posterior vitreous separation which facilitates good vitrectomy. The main aims of secondary repair are:

- To clear opacities of the media such as cataract and vitreous haemorrhage in order to improve vision.
- To stabilize abnormal vitreoretinal interactions and thereby prevent long-term sequelae such as tractional retinal detachment.

Extraocular foreign bodies

Small foreign bodies such as particles of steel, coal or sand often impact on the corneal or conjunctival surface. Subsequent to such impact, such foreign bodies may:

- Be washed along the tear film into the lacrimal drainage system.
- Adhere to the superior palpebral conjunctiva in the subtarsal sulcus and abrade the cornea with every blink. A pathognomonic pattern of linear corneal abrasions may be seen (Fig. 19.56). A subtarsal foreign body is easily missed unless the upper lid is everted.

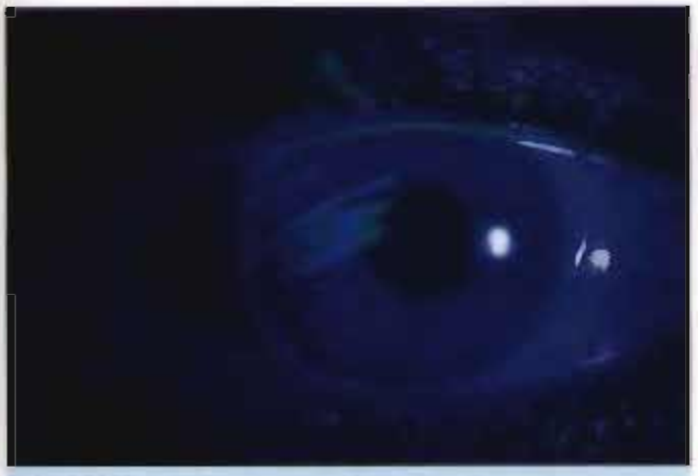

Fig. 19.56
Linear corneal abrasions stained with fluorescein due to a subtarsal foreign body

- Ascend and lodge in the superior conjunctival fornix and produce chronic conjunctivitis. Such a foreign body is easily missed, unless the lid is double-everted and the fornix is examined.
- Impact in the bulbar conjunctiva.
- Impact in the corneal epithelium or stroma to a depth proportional to the velocity of the foreign body.
- A very high-velocity foreign body may penetrate the cornea or sclera and lodge intraocularly.

Corneal foreign bodies

1. **Clinical features.** Corneal foreign bodies are extremely common and cause considerable irritation. Leukocytic infiltration may also develop around any foreign body of some duration. If a foreign body is allowed to remain, there is a risk of secondary infection and corneal ulceration. Mild secondary uveitis is common with irritative miosis and photophobia. Ferrous foreign bodies of even a few days' duration often result in rust staining of the bed of the abrasion.
2. **Management**
   a. Careful slit-lamp examination is essential to locate the exact position and depth of the foreign body.
   b. The foreign body is removed under slit-lamp visualization using a sterile 26-gauge needle. Magnetic removal may be useful for a deeply embedded metallic foreign body. A residual 'rust ring', is easiest to remove with a sterile 'burr'.
   c. Antibiotic ointment is instilled together with a cycloplegic and/or ketorolac to promote comfort.

NB: Any discharge, infiltrate or significant uveitis should raise suspicion of secondary bacterial infection; subsequent management should be as for a corneal ulcer. Metallic foreign bodies are often sterile due to acute rise in temperature during transit through the air; organic and stone foreign bodies however, carry a higher risk of infection.

Intraocular foreign bodies

An intraocular foreign body may traumatize the eye mechanically, introduce infection or exert other toxic effects on the intraocular structures. Once in the eye, the foreign body may lodge in any of the structures it encounters: thus it may be located anywhere from the anterior chamber to the retina and choroid. Notable mechanical effects include cataract formation secondary to capsular injury, vitreous liquefaction, and retinal haemorrhages and tears. Stone and organic foreign bodies are particularly prone to result in infection. Many substances including glass, many plastics, gold and silver are inert. However, iron and copper may undergo dissociation and result in siderosis and chalcosis respectively.

Siderosis

Perhaps the commonest foreign body is a piece of steel. An intraocular ferrous foreign body undergoes dissociation resulting in the deposition of iron in the intraocular epithelial structures, notably the lens epithelium and the retina, where it exerts a toxic effect on cellular enzyme systems, with resultant cell death. Features of siderosis include anterior capsular cataract, consisting of radial iron deposits on the anterior lens capsule, reddish-brown staining of the iris (Fig. 19.57), secondary glaucoma due to trabecular damage and pigmentary retinopathy, the last of which has the most profound effects on vision. Electroretinography manifests progressive attenuation of the b-wave over time.

Chalcosis

The ocular reaction to an intraocular foreign body with a high copper content involves a violent endophthalmitis-like picture, often with progression to phthisis bulbi. On the other hand, an alloy such as brass or bronze, with a relatively low copper content, results in chalcosis. Electrolytically dissociated copper becomes deposited intraocularly, resulting in a picture similar to that seen in Wilson disease. Thus a

Fig. 19.57
Cataract and iris staining due to siderosis (Courtesy of J. Salmon)

Kayser–Fleischer ring develops (*see* Fig. 5.140), as does an anterior 'sunflower' cataract. Retinal deposition results in golden plaques visible ophthalmoscopically. Since copper is less retinotoxic than iron, degenerative retinopathy does not develop and visual function may be preserved.

Initial management

1. **Accurate history** is vital to determine the origin of the foreign body; it may be helpful for the patient to bring any causative objects such as a chisel.
2. **Ophthalmic examination** is performed, paying special attention to any possible sites of entry or exit. Topical fluorescein may be helpful to identify an entry wound. Alignment and projection of identified wounds may allow logical deduction of the probable location of a foreign body. Gonioscopy and funduscopy must be performed. Associated signs such as lid laceration and damage to anterior segment structures must be noted.
3. **CT** with axial and coronal cuts is used to detect and localize metallic intraocular foreign bodies (*see* Fig. 19.23), providing cross-sectional images with a sensitivity and specificity that are superior to plain radiography and ultrasonography.

> ***NB:*** MRI scanning is contraindicated in the context of a metallic intraocular foreign body.

Technique of removal

1. **Magnet** removal is as follows:
   a. A sclerotomy is performed adjacent to the foreign body (Fig. 19.58a).
   b. Low-intensity diathermy is applied to the choroid to prevent bleeding (Fig. 19.58b).
   c. The foreign body is removed with the magnet (Fig. 19.58c).
   d. Cryotherapy may be applied to the induced retinal tear and adjacent retina (Fig. 19.58d).
   e. Scleral buckling (Fig. 19.58e) may be performed to reduce the risk of retinal detachment, but this is optional.
2. **Forceps** removal may be used for non-magnetic foreign bodies and magnetic foreign bodies that cannot be safely removed with a magnet.
   a. A complete pars plana vitrectomy is performed (Fig. 19.59a).
   b. Intraocular forceps are introduced (Fig. 19.59b).
   c. A small foreign body may be removed through the pars plana.
   d. A large foreign body in the aphakic eye may be removed by holding it in the pupillary space (Fig. 19.60a), inserting a keratome (Fig. 19.60b) and delivering it through a limbal incision (Fig. 19.60c).

> ***NB:*** Prophylaxis of endophthalmitis with intravitreal antibiotics is required in high-risk cases such as soil-contaminated or vegetable matter foreign bodies.

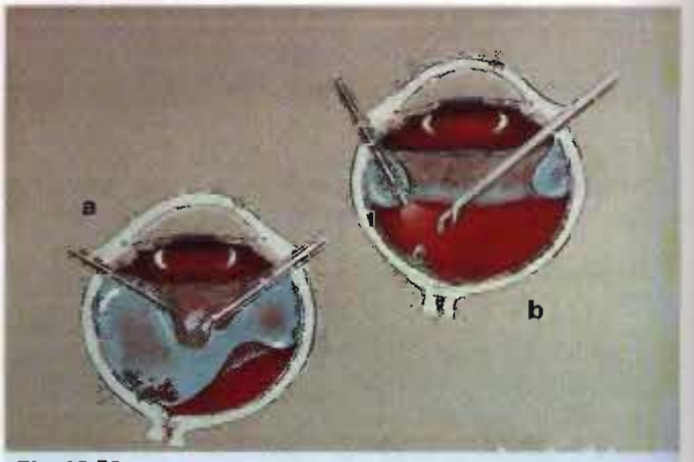

Fig. 19.59
Forceps removal of intraocular foreign body through the pars plana (see *text*) (Courtesy of Wilmer Institute)

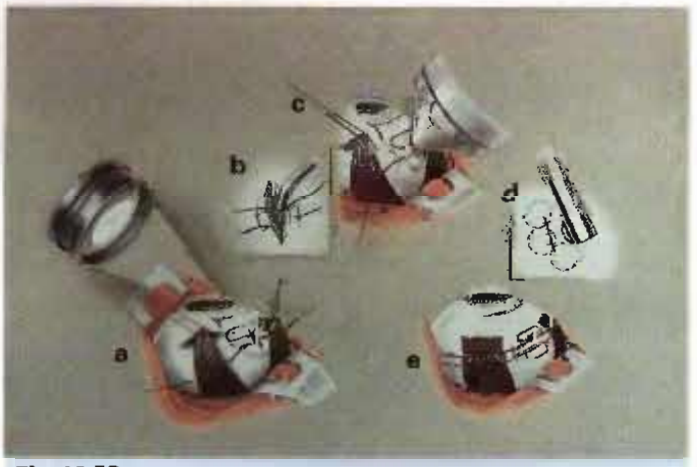

Fig. 19.58
Magnet removal of intraocular foreign body (see *text*) (Courtesy of Wilmer Institute)

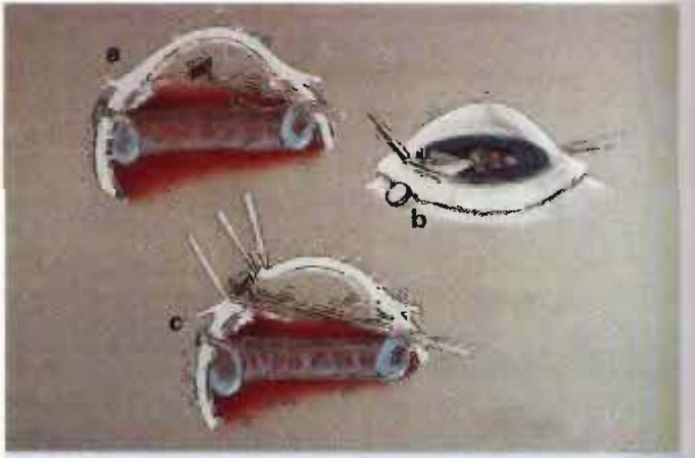

Fig. 19.60
Forceps removal of intraocular foreign body through the limbus (see *text*) (Courtesy of Wilmer Institute)

Fig. 19.61
Extremely damaged globe where primary enucleation is justifiable

Enucleation

Primary enucleation should be performed only for very severe injuries, with no prospect of retention of vision when it is impossible to repair the sclera (Fig. 19.61). Secondary enucleation may be considered following primary repair if the eye is severely and irreversibly damaged, particularly if it is also unsightly and uncomfortable. The time delay also allows the patient valuable time to mentally and emotionally adapt to the prospect of losing an eye. Based on anecdotal evidence, it has been recommended that enucleation should be performed within 10 days of the original injury in order to prevent the very remote possibility of sympathetic ophthalmitis. However, objective evidence for this is lacking.

Sympathetic ophthalmitis

Sympathetic ophthalmitis is a very rare, *bilateral*, granulomatous panuveitis which occurs after penetrating ocular trauma usually associated with uveal prolapse or, less frequently, following intraocular surgery. The traumatized eye is referred to as the *exciting* eye and the fellow eye, which also develops uveitis, is called the *sympathizing* eye.

Fig. 19.62
Mutton fat keratic precipitates in sympathetic ophthalmitis

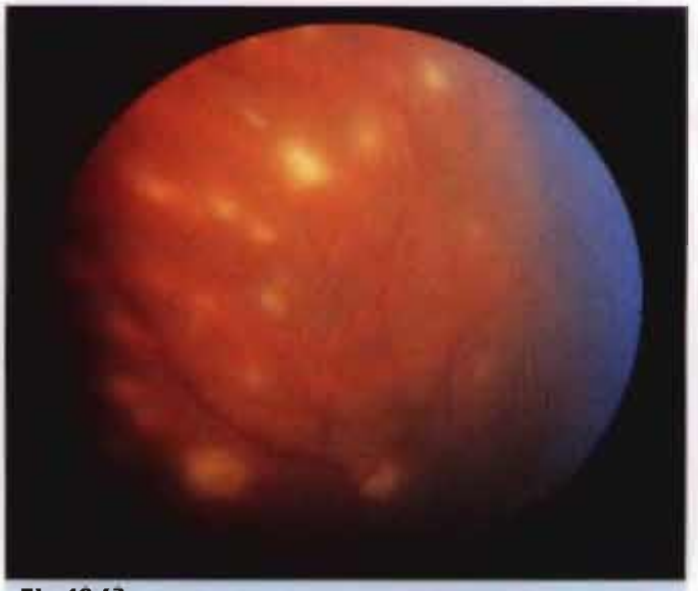

Fig. 19.63
Multifocal choroiditis in sympathetic ophthalmitis (Courtesy of J. Salmon)

1. **Presentation** in 65% of cases is between 2 weeks and 3 months after initial injury; 90% of all cases occur within the first year.
2. **Signs**
   - The exciting eye shows evidence of the initial trauma and is frequently very red and irritable.
   - The sympathizing eye becomes photophobic and irritable.
   - Both eyes then develop a chronic granulomatous anterior uveitis with iris nodules and mutton fat keratic precipitates (Fig. 19.62).
   - Optic disc swelling and multifocal choroiditis involve the entire fundus (Fig. 19.63).
3. **Course.** Rarely the uveitis runs a relatively mild and self-limiting course. Usually, however, the intraocular inflammation becomes chronic and, unless appropriately treated, may lead to cataract, glaucoma and phthisis bulbi.
4. **Treatment** with systemic steroids is usually effective and the long-term visual prognosis good. A variety of steroid-sparing immunosuppressive agents are also beneficial.

Chemical injuries

Introduction

Causes

Chemical injuries range in severity from trivial to potentially blinding. The majority are accidental and a few the result of assault. Two-thirds of accidental burns occur at work and the remainder at home. Alkali burns are twice as common as

acid burns since alkalis are more widely used at home and in industry. The most common involved alkalis are ammonia, sodium hydroxide and lime. The commonest acids implicated are sulphuric, sulphurous, hydrofluoric, acetic, chromic and hydrochloric. The severity of a chemical injury is related to the properties of the chemical, the area of affected ocular surface, duration of exposure (retention of particulate chemical on the surface of the globe) and related effects such as thermal damage. Alkalis tend to penetrate deeper than do acids, which coagulate surface proteins, resulting in a protective barrier. Ammonia and sodium hydroxide may produce severe damage because of rapid penetration. Hydrofluoric aid used in glass etching and cleaning also tends to rapidly penetrate the eye, while sulphuric acid may be complicated by thermal effects and high-velocity impact after car battery explosions.

Pathophysiology

1. **Ocular damage** by severe chemical injuries occurs in the following order:
   - Necrosis of the conjunctival and corneal epithelium with disruption and occlusion of the limbal vasculature. Loss of limbal stem cells may subsequently result in conjunctivalization and vascularization of the corneal surface or persistent corneal epithelial defects with sterile corneal ulceration and perforation. Other long-term effects include ocular surface wetting disorders, symblepharon formation and cicatricial entropion.
   - Deeper penetration causes breakdown and precipitation of glycosaminoglycans and stromal corneal opacification.
   - Anterior chamber penetration results in iris and lens damage.
   - Ciliary epithelial damage impairs secretion of ascorbate, which is required for collagen production and corneal repair.
   - Hypotony and phthisis bulbi may ensue.
2. **Healing** of the corneal epithelium and stroma is as follows:
   - The epithelium heals by migration of epithelial cells which originate from limbal stem cells.
   - Damaged stromal collagen is phagocytosed by keratocytes and new collagen is synthesized.

Management

Emergency treatment

A chemical burn is the only eye injury that requires immediate treatment without first taking a history and performing a careful examination. Immediate treatment is as follows:

1. **Copious irrigation** is crucial to minimize duration of contact with the chemical and normalize the pH in the conjunctival sac as soon as possible. Normal saline (or equivalent) should be used to irrigate the eye for 15–30 minutes or until pH is normalized.
2. **Double-eversion of the eyelids** should be performed so that any retained particulate matter trapped in the fornices, such as lime or cement, may be removed.
3. **Debridement** of necrotic areas of corneal epithelium should be performed to allow for proper re-epithelialization.

Grading of severity

Acute chemical injuries are then graded to plan appropriate subsequent treatment and afford an indication of likely ultimate prognosis. Grading is performed on the basis of corneal clarity and severity of limbal ischaemia. The latter is assessed by observing the patency of the deep and superficial vessels at the limbus (Fig. 19.64).

1. **Grade I**: clear cornea and no limbal ischaemia (excellent prognosis).
2. **Grade II**: hazy cornea but with visible iris details (Fig. 19.65) and less than one-third (120°) of limbal ischaemia (good prognosis).

Fig. 19.64
Severe limbal ischaemia following a recent chemical injury

Fig. 19.65
Grade II chemical injury with corneal haze but visible iris details

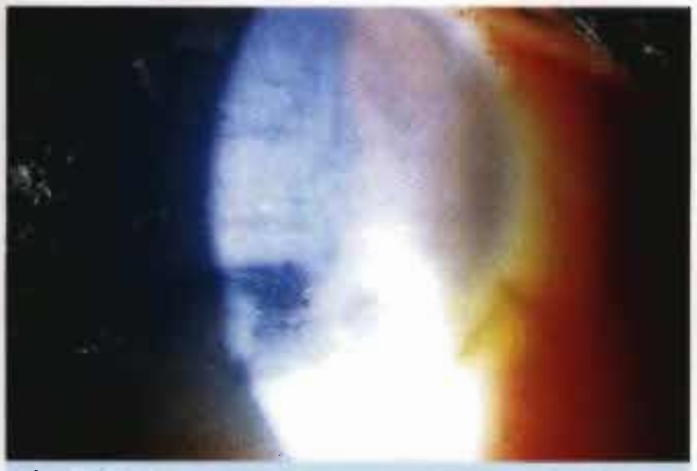

Fig. 19.66
Grade III chemical injury with corneal haze obscuring iris details

Fig. 19.67
Grade IV chemical injury with totally opaque cornea

3. **Grade III**: total loss of corneal epithelium, stromal haze obscuring iris details (Fig. 19.66) and between one-third and half (120° to 180°) of limbal ischaemia (guarded prognosis).
4. **Grade IV**: opaque cornea and more than half (>180°) of limbal ischaemia (Fig. 19.67) (very poor prognosis).

Other features to note at initial assessment are the extent of corneal and conjunctival epithelial loss, iris changes, status of the lens and intraocular pressure.

Medical treatment

Mild (grades I and II) injuries are treated with a short course of topical steroids, cycloplegics and prophylactic antibiotics for about 7 days. The main aims of treatment of more severe burns are to reduce inflammation, promote epithelial regeneration and prevent corneal ulceration.

i. **Steroids** reduce inflammation and neutrophil infiltration. However, they also impair stromal healing by reducing collagen synthesis and inhibiting fibroblast migration. For this reason topical steroids may be used initially but must be tailed off after 7–10 days when sterile corneal ulceration is most likely to occur. They may be replaced by topical NSAIDs, which do not affect keratocyte function.
2. **Ascorbic acid** reverses a localized tissue scorbutic state and improves wound healing by promoting the synthesis of mature collagen by corneal fibroblasts. Topical sodium ascorbate 10% is given 2-hourly in addition to a systemic dose of 2 g q.i.d.
3. **Citric acid** is a powerful inhibitor of neutrophil activity and reduces the intensity of the inflammatory response. Chelation of extracellular calcium by citrate also appears to inhibit collagenase. Topical sodium citrate 10% is given 2-hourly for about 10 days. The aim is to eliminate the second wave of phagocytes, which normally occurs 7 days after the injury.
4. **Tetracyclines** are collagenase inhibitors and also inhibit neutrophil activity and reduce ulceration. They are administered both topically and systemically (e.g. doxycycline 100 mg b.d.).

Surgery

1. **Early surgery** may be necessary to revascularize the limbus, restore the limbal cell population and re-establish the fornices. One or more of the following procedures may be used:
   - Advancement of Tenon capsule and suturing to the limbus is aimed at re-establishing limbal vascularity, thus preventing the development of corneal ulceration.
   - Limbal stem cell transplantation from the patient's other eye (autograft) or from a donor (allograft) is aimed at restoring normal corneal epithelium.
   - Amniotic membrane grafting to promote epithelialization and suppression of fibrosis.
2. **Late surgery** may involve the following procedures:
   - Division of conjunctival bands (Fig. 19.68) and symblepharon (Fig. 19.69).

Fig. 19.68
Conjunctival adhesions following chemical injury

Fig. 19.69
Symblepharon following chemical injury

- Conjunctival or mucous membrane grafts.
- Correction of eyelid deformities.
- Keratoplasty should be delayed for at least 6 months and preferably longer to allow maximal resolution of inflammation.
- Keratoprostheses (*see* Fig. 6.15) may be required in very severely damaged eyes because the results of conventional grafting are poor.

CHAPTER 20

Systemic Diseases

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Acromegaly

Acromegaly is caused by excessive growth hormone (GH) occurring during adult life, after epiphyseal closure, and is almost invariably due to a secreting pituitary acidophil adenoma. (Hypersecretion of growth hormone in childhood, prior to epiphyseal closure, results in gigantism.)

1. **Presentation** is in the fourth to fifth decades.
2. **Signs**
   - *a. Skin.* Hyperhidrosis, seborrhoea, acne and in females hirsutism.
   - *b. Face.* Coarseness of features: thick lips, exaggerated nasolabial folds, prominent supraorbital ridges (Fig. 20.1) and enlargement of the lower jaw (prognathism) (Fig. 20.2) with dental malocclusion.
   - *c. Enlargement* of the head, hands, feet, tongue (Fig. 20.3) and internal organs.
3. **Complications** include osteoarthritis (Fig. 20.4), carpal tunnel syndrome, cardiomyopathy, hypertension, respiratory disease, diabetes mellitus, gonadal dysfunction and neuropathy.
4. **Diagnostic tests.** The diagnosis may be confirmed by noting GH levels in response to an oral glucose tolerance test. Normal individuals manifest suppression of GH levels to below 2 mU/L. However, in acromegaly, GH levels do not fall, and may paradoxically rise.
5. **Treatment** options include bromocriptine (a long-acting dopamine agonist), radiotherapy (external beam or by implantation of yttrium rods in the pituitary) and transsphenoidal hypophysectomy.

Fig. 20.1
Acromegaly

Fig. 20.2
Plain skull radiograph of acromegaly showing an enlarged mandible with widening of the mandibular angle (prognathism), enlarged frontal sinus, thickening of the skull vault and an expanded pituitary fossa (Courtesy of S. Ghiacy)

Fig. 20.3
Macroglossia in acromegaly

Fig. 20.4
Plain radiograph of the hands in acromegaly showing lips and hooks of the terminal phalanges, enlarged bones with prominent muscle attachments and early osteoarthritic changes (Courtesy of S. Ghiacy)

6. **Ophthalmic features**
   a. *Common.* Bitemporal hemianopia and optic atrophy.
   b. *Rare.* Angioid streaks and see-saw nystagmus of Maddox.

Acquired immunodeficiency syndrome

Acquired immunodeficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV), which is predominantly transmitted by sexual intercourse and occasionally by contaminated blood or needles. On a worldwide basis, heterosexual intercourse is the predominant mode of transmission; in the Western world, however, AIDS is commonly transmitted by homosexual contact. Transmission may also occur transplacentally or via breast milk. Infection with HIV is typically followed by a latent period, after which develop the clinical manifestations of AIDS. HIV targets CD4+T-(helper) lymphocytes, which are vital to the initiation of the immune response to pathogens. A steady decline in the absolute number of CD4+T-lymphocytes therefore occurs, resulting in progressive immune deficiency, particularly that of cell-mediated immunity. Regular estimation of the CD4+T count is therefore a useful measure of disease progression. Apart from immunodeficiency, HIV also has the property of mediating direct damage to the central nervous system.

1. **Presentation**
   a. ***Acute seroconversion illness.*** HIV infection is sometimes followed a few weeks later by constitutional symptoms such as fever, headache, malaise and a maculopapular rash, associated with generalized lymphadenopathy, soon after which anti-HIV antibodies appear.
   b. ***An asymptomatic phase***, often lasting many years, then follows, during which steady depletion of CD4+T-lymphocytes occurs.
   c. *Symptomatic HIV infection* (AIDS) then follows, characterized by immunosuppression with opportunistic infections and tissue damage directly due to HIV infection.
2. **Opportunistic infections** in AIDS include:
   a. *Protozoan.* Toxoplasma, cryptosporidium, microsporidium and *Pneumocystis carinii*.
   b. *Viral.* Cytomegalovirus, herpes simplex and zoster, molluscum contagiosum and Epstein–Barr.
   c. *Fungal.* Cryptococcus, candida (Fig. 20.5) and histoplasma.
   d. *Bacterial. Mycobacterium tuberculosis, Mycobacterium avium*, staphylococci, streptococci, *Haemophilus* and *Bartonella henselae*.
3. **Tumours** include Kaposi sarcoma (Fig. 20.6), non-Hodgkin B-cell lymphoma and squamous cell carcinoma of the cervix and anus.
4. **Other manifestations** include HIV wasting syndrome, encephalopathy and progressive multifocal leucoencephalopathy.
5. **Diagnostic tests.** Serological testing for HIV infection should be performed only with informed consent after proper counselling, due to the profound implications of a positive result. HIV is confirmed most commonly by the demonstration of anti-HIV antibodies in the serum, by the ELISA and western blot tests. 'Seroconversion' may take 3 months or longer to occur following exposure to the virus, sometimes necessitating serial testing in individuals at high risk. Subsequent to the establishment of HIV positivity, CD4+T-lymphocyte counts are measured every 3 months. A CD4+T-lymphocyte count $< 200/mm^3$ implies a high risk of HIV-related disease. AIDS is diagnosed when an HIV-positive subject develops one or more of a defined list of indicator diseases (Table 20.1).
6. **Treatment.** Although there is no cure for AIDS, the progression of disease can be slowed by a number of drugs. The aim of treatment is to reduce the plasma viral load. Ideally therapy should be commenced before the development of irreversible damage to the immune system.
   a. ***Indications*** for commencement of anti-HIV therapy include:
      - Symptomatic HIV disease.
      - CD4+T-lymphocyte count $< 300/mm^3$.
      - Rapidly falling CD4+T-lymphocyte count.
      - Viral load $> 10{,}000$/ml of plasma.
   b. ***Drug*** treatment is with 'highly active antiretroviral therapy' (HAART), which involves two nucleoside reverse

Fig. 20.5
Oral candidiasis in AIDS

Fig. 20.6
Kaposi sarcoma in AIDS

Table 20.1 AIDS-defining diagnoses (1993 Classification, Europe)

- Candidiasis of bronchi, trachea, lungs or oesophagus
- Cervical carcinoma, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcus, extrapulmonary
- Cryptosporidiosis, with diarrhoea for >1 month
- Cytomegalovirus disease other than in liver, spleen or lymph nodes
- Encephalopathy, HIV-related
- Herpes simplex ulcers for 1 month or bronchitis, pneumonitis or oesophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, with diarrhoea for >1 month
- Kaposi sarcoma
- Lymphoid interstitial pneumonitis
- *Mycobacterium avium* complex or *M. kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Pneumonia, recurrent
- Progressive multifocal leucoencephalopathy
- Salmonella (non-typhoid) septicaemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV (weight loss >10% baseline with no other identified cause)

transcriptase inhibitors with either a non-nucleoside reverse transcriptase inhibitor or one or two protease inhibitors.

- Nucleoside reverse transcriptase inhibitors include zidovudine, lamivudine and zalcitabine.
- Protease inhibitors include amprenavir, indinavir and nelfinadir.
- Non-nucleoside reverse transcriptase inhibitors include efavirenz and nevirapine.

NB: Antiretroviral therapy is continuously evolving and should therefore be left to a trained physician.

7. Ophthalmic features

*a. **Eyelids.*** Kaposi sarcoma, multiple molluscum lesions and severe herpes zoster ophthalmicus.

*b. **Orbit.*** Cellulitis usually from contiguous sinus infection and B-cell lymphoma.

*c. **Conjunctiva.*** Kaposi sarcoma, squamous cell carcinoma and microangiopathy.

*d. **Cornea.*** Keratitis due to microsporidium, herpes simplex and herpes zoster.

*e. **Keratoconjunctivitis sicca.***

*f. **Anterior uveitis.***

*g. **HIV retinopathy*** (cotton wool spots).

*h. **Retinitis.*** Cytomegalovirus, varicella zoster (progressive outer retinal necrosis) and toxoplasma.

*i. **Choroiditis.*** Pneumocystis and cryptococcus.

*j. **B-cell intraocular lymphoma.***

Ankylosing spondylitis

Ankylosing spondylitis (AS) is a spondarthropathy, primarily involving inflammation, calcification and finally ossification of ligaments and capsules of joints, with resultant bony ankylosis of the axial skeleton. It typically affects males, 90% of whom are HLA-B27 positive.

1. Presentation is in early adulthood with insidious onset of pain and stiffness in the lower back or buttocks. This is initially worse after inactivity, but may be aggravated by weight bearing.

2. Signs

*a. **Arthritis.*** In order of frequency, the joints most affected are the sacro-iliac, spine, hips, ribs and shoulders.

Fig. 20.7
Limitation of spinal flexion in advanced ankylosing spondylitis

Fig. 20.8
Severe spinal involvement in ankylosing spondylitis with bony bridging by syndesmophytes ('bamboo spine') (Courtesy of S. Ghaey)

Progressive limitation of spinal movements occurs (Fig. 20.7); the spine characteristically becomes fixed in flexion. Reduced mobility of the thoracic cage may predispose to pulmonary infection.

b. Enthesopathy of the plantar fascia and Achilles tendon.

3. **Associations.** Inflammatory bowel disease (colitic arthritis).
4. **Complications.** Apical pulmonary fibrosis, aortic incompetence and cardiac conduction defects.
5. **Diagnostic tests.** The ESR is raised. Radiology of the sacro-iliac joints reveals juxta-articular osteoporosis in the early stages, later followed by sclerosis and bony obliteration of the joint. The spinal ligaments may also manifest calcification ('bamboo spine') (Fig. 20.8), as may other joints involved by the inflammatory process.
   NB: Radiological changes often pre-date clinical symptoms.
6. **Treatment** options include physiotherapy, NSAIDs, sulphasalazine and intra-articular steroid injections. Surgical correction of bony deformities may be necessary.
7. **Ophthalmic features.** Acute anterior uveitis in 30%.

Atopic eczema

Atopic eczema (dermatitis) is an idiopathic, often familial, skin condition, which may be associated with asthma and hay fever.

1. **Presentation** is with intense pruritus usually in infancy, but may be at any age.
2. **Signs**
   a. Facial eczema is usually seen in infants and consists of itchy, dry, erythematous papules (Fig. 20.9).
   b. Flexural eczema (Fig. 20.10) usually develops later with symmetrical involvement of the elbow and knee flexures, wrists and ankles by dry, lichenified or excoriated skin.
3. **Treatment** options include emollients, coal-tar preparations and topical steroids.
4. **Ophthalmic features**
   a. Common. Madarosis and staphylococcal blepharitis.

Fig. 20.9
Infantile eczema

Fig. 20.10
Adult eczema

b. Uncommon. Chronic keratoconjunctivitis, keratoconus and early-onset cataract.
c. Rare. Retinal detachment.

Behçet disease

Behçet disease is an idiopathic, recurrent, multisystem disease. It typically affects young men from the eastern Mediterranean region and Japan and is associated with HLA-B51 and its subtype HLA-Bw51.

1. **Presentation** is in the third to fourth decades with localized lesions such as aphthous ulceration.
2. **Major diagnostic criteria**
   a. Recurrent oral aphthous stomatitis is universal. A typical aphthous ulcer is painful and shallow with a yellowish necrotic base. They occur in crops on the tongue (Fig. 20.11), gums, lips and buccal mucosa.
   b. Skin lesions include erythema nodosum (Fig. 20.12), acneiform (Fig. 20.13), subcutaneous thrombophlebitis, a papulo-vesiculo-pustular rash and hypersensitivity.

Fig. 20.11
Aphthous ulceration in Behçet disease

The latter can be tested with a 'prick' (pathergy) test, in which a pustule appears after puncturing the skin with a needle (Fig. 20.14) or by stroking the skin and demonstrating the appearance of corresponding lines (dermatographism) (Fig. 20.15).

Fig. 20.12
Erythema nodosum-like skin lesions in Behçet disease (Courtesy of B. Noble)

Fig. 20.13
Acneiform skin lesions in Behçet disease (Courtesy of B. Noble)

Fig. 20.14
Pustule formed following pricking in Behçet disease (positive pathergy test) (Courtesy of B. Noble)

Fig. 20.15
Cutaneous hypersensitivity demonstrated by stroking the skin (dermatographism) in Behçet disease (Courtesy of B. Noble)

Fig. 20.16
Genital ulceration in Behçet disease

c. ***Recurrent genital ulceration*** of the penis (Fig. 20.16) and scrotum in males and of the labia and vagina in females.
d. ***Uveitis***, both anterior and posterior.

Fig. 20.17
Dilated superficial veins secondary to deep obliterative thrombophlebitis in Behçet disease. (Courtesy of B. Noble)

3. **Minor diagnostic criteria**
   a. *Arthritis* involving the knees, ankles and occasionally the sacro-iliac joints.
   b. *Epididymitis*.
   c. *Intestinal ulceration*.
   d. *Vascular*. Obliterative thrombophlebitis of superficial and deep veins (Fig. 20.17), large vessel arterial occlusion and aneurysm formation.
   e. *Neurological*. Brain stem syndromes and meningoencephalitis.
4. **Complete Behçet disease**. Four major criteria occurring simultaneously or at different times.
5. **Incomplete Behçet disease**. One of the following:
   - Three major criteria.
   - Two major plus two minor criteria.
   - Uveitis plus another major criterion.
   - Uveitis plus two minor criteria.
6. **Treatment**
   a. *Topical* tetracycline or steroids for local lesions such as oral or genital ulcers.
   b. *Systemic* therapeutic options include steroids, often in combination with colchicine, azathioprine, cyclosporin, chlorambucil and levamisole.
7. **Ophthalmic features**
   a. *Common*. Anterior uveitis, vitritis and retinitis.
   b. *Uncommon*. Occlusive retinal periphlebitis, periarteritis and retinal oedema.

Carotid stenosis

Carotid stenosis involves atheromatous narrowing, often associated with ulceration, at the bifurcation of the common carotid artery. The irregularity of the vessel wall may act as a source of cerebral and retinal emboli composed of platelets and fibrin (white emboli) or tiny fragments of atheromatous material (Hollenhorst plaques).

1. **Presentation** is in the seventh to ninth decades with:
   - Transient retinal ischaemic attacks (amaurosis fugax).
   - Retinal artery occlusion.
   - Transient cerebral ischaemic attacks (TIA).
   - Stroke.
   - Ocular ischaemic syndrome.
   - Asymmetrical diabetic retinopathy—the ipsilateral eye tends to be relatively spared.
2. **Signs**
   a. *Palpation* of the cervical carotid arteries should be done gently to avoid dislodging a thrombus. Severe or complete stenosis is associated with a diminished or absent carotid pulse. Other peripheral pulses may also be diminished in generalized atherosclerosis.
   b. *Auscultation* over a partial stenosis gives rise to a bruit, best detected with the bell of the stethoscope. It is important to auscultate along the entire length of the artery and to ask the patient to hold his breath. The most ominous bruit is one that is high-pitched and soft because it indicates tight stenosis. When the lumen is narrowed by 90% or more, the bruit disappears.
3. **Diagnostic tests**
   a. *Duplex scanning* is a non-invasive screening test involving a combination of high-resolution real-time ultrasonography with Doppler flow analysis (Fig. 20.18).
   b. *Magnetic resonance angiography* is non-invasive and accurate (Fig. 20.19).
   c. *Carotid arteriography* is the most accurate method (Fig. 20.20) but carries a significant risk of complications. Resolution can be further improved by digitally removing (subtracting) the distracting background, leaving only the arterial image (Fig. 20.21).
4. **Treatment** is aimed at preventing stroke and permanent visual impairment by the following:
   a. *General measures* addressing associated risk factors such as smoking, hypertension, diabetes, obesity, hypercholesterolaemia and cardiac arrhythmias.

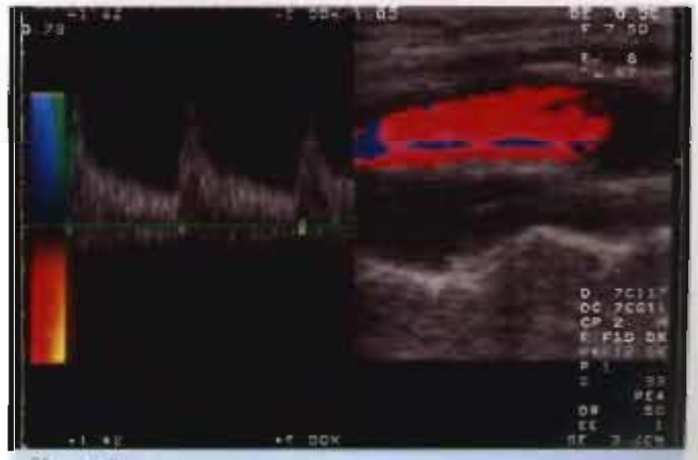

Fig. 20.18
Colour Doppler ultrasonogram showing carotid stenosis

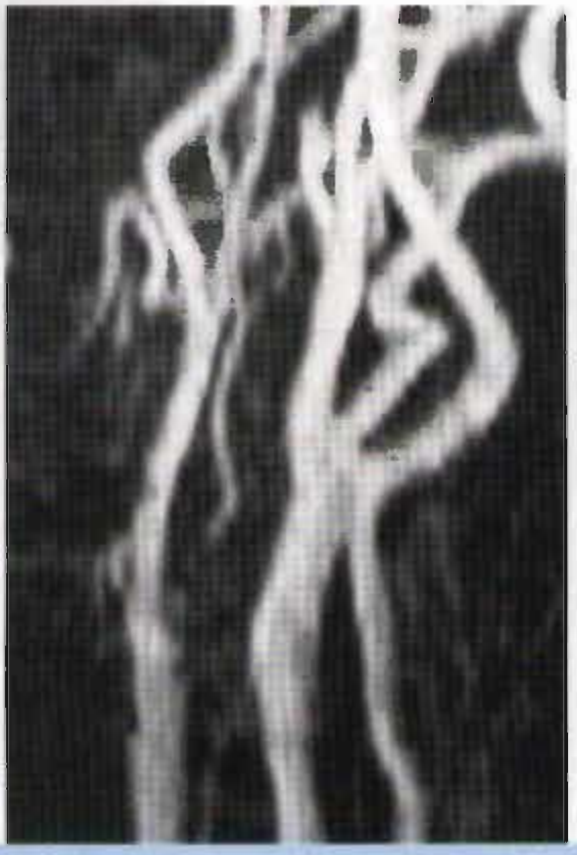

Fig. 20.19
MRA showing severe stenosis of the right internal carotid artery (Courtesy of D. Thomas)

Fig. 20.21
Digital subtraction arteriogram showing severe stenosis of the right internal carotid artery (Courtesy of D. Thomas)

Fig. 20.20
Arteriogram without subtraction showing severe stenosis of the right internal carotid artery (Courtesy of D. Thomas)

   b. Antiplatelet therapy.
      - Aspirin 75–300 mg daily.
      - Combined aspirin and dipyridamole (Persantin) 200 mg daily, if aspirin alone is ineffective.
      - Clopidogrel (Plavix) 75 mg daily if other measures fail.
   c. Oral anticoagulants such as warfarin, if TIAs continue despite antiplatelet therapy.
   d. Carotid endarterectomy (Fig. 20.22) is indicated in patients with symptomatic stenosis greater than 70%.
5. **Ophthalmic features**
   a. Common. Amaurosis fugax.
   b. Uncommon. Hollenhorst plaques and retinal artery occlusion.
   c. Rare. Hypotensive (slow flow) retinopathy and ocular ischaemic syndrome

Cat-scratch disease

Cat-scratch disease (fever) is a subacute infection caused by a small Gram-negative bacillus, *Bartonella henselae*, transmitted by a scratch or bite of an infected animal, often a cat.

1. **Presentation** is at any age with a pustule at the site of inoculation followed by constitutional symptoms, lymphadenopathy and erythema nodosum.

Fig. 20.22
Scar following carotid endarterectomy

2. **Disseminated disease** is rare but may affect immunocompromised individuals. It is characterized by encephalitis, hepatitis, pneumonia, splenomegaly, splenic abscess formation and osteomyelitis.
3. **Diagnostic tests** include blood cultures and immunofluorescent antibody titres.
4. **Treatment** is with oral doxycycline and rifampicin; the organism is also sensitive to ciprofloxacin and co-trimoxazole.
5. **Ophthalmic features**
   a. Uncommon. Neuroretinitis.
   b. Rare. Parinaud oculoglandular syndrome, intermediate uveitis, acute multifocal retinitis, retinal periphlebitis and exudative retinal detachment.

Chlamydial genital infection

Chlamydial genital infection is sexually transmitted and caused by serotypes D–K of *Chlamydia trachomatis*.

1. **In males** chlamydial infection is the most common cause of 'non-specific urethritis' (NSU) and 'non-gonococcal urethritis' (NGU). It may also cause epididymitis and act as a trigger for Reiter disease.
2. **In females** chlamydia may cause abacterial pyuria, cervicitis, salpingitis, peritonitis and perihepatitis (Fitz-Hugh–Curtis syndrome). Chronic salpingitis may result in infertility.
3. **Treatment**. Doxycycline 100 mg b.d. for 7 days or a single dose of azithromycin 1000 mg.
4. **Ophthalmic features**
   a. Uncommon. Adult conjunctivitis.
   b. Rare. Neonatal conjunctivitis.

Cicatricial pemphigoid

Cicatricial pemphigoid (benign mucous membrane pemphigoid) is a chronic autoimmune (type 2 hypersensitivity) disease characterized by recurrent blisters of the mucous membranes and skin. It affects women twice as often as men and is associated with an increased prevalence of HLA-B12.

Fig. 20.23
Oral involvement in cicatricial pemphigoid

1. **Presentation** is in the seventh to eighth decades with ocular or mucocutaneous lesions or both.
2. **Signs**
   a. Mucosal blisters, most frequently oral (Fig. 20.23), rupture within a day or two, leaving erosions and ulcers which heal without scarring. Other sites include the nose, larynx, oesophagus, anus, vagina, glans penis and urethra; ulcers at these sites heal with scarring and may result in stricture formation.
   b. Skin lesions are less common and are of two types.
   - Recurrent, non-scarring blisters which may involve the groins and/or extremities (Fig. 20.24) and may occasionally become generalized.
   - Sparse, localized erythematous plaques associated with recurrent scarring blisters on the scalp and skin near affected mucous membranes.
3. **Treatment**
   a. Local oral lesions may be treated with topical steroids.
   b. Widespread involvement, particularly of the eyes, requires systemic steroids, azathioprine, dapsone or intravenous immunoglobulin.
4. **Ophthalmic features.** Cicatrizing conjunctivitis in the vast majority of cases.

Fig. 20.24
Cutaneous involvement in cicatricial pemphigoid

Fig. 20.26
Glossitis in Crohn disease

Crohn disease

Crohn disease (regional ileitis) is an idiopathic, chronic, relapsing disease characterized by multifocal, full-thickness, non-caseating granulomatous inflammation of the intestinal wall. It most frequently involves the ileocaecal region (Fig. 20.25) but any area of the bowel, including the mouth, may be affected.

1. **Presentation** is in the second to third decades with fever, weight loss, diarrhoea and abdominal pain.
2. **Extra-intestinal manifestations**
   a. Oral. Glossitis (Fig. 20.26) and aphthous ulceration.
   b. Cutaneous. Erythema nodosum, pyoderma gangrenosum (Fig. 20.27) and psoriasis.
   c. Skeletal. Finger clubbing, acute peripheral arthritis, sacroiliitis and ankylosing spondylitis.
3. **Complications** include intestinal obstruction due to stricture formation (Fig. 20.28), perirectal fistulae, abscesses and fissures, and liver disease.
4. **Diagnostic tests** include endoscopy and biopsy.

Fig. 20.27
Pyoderma gangrenosum in Crohn disease

5. **Treatment** options include nutritional support, steroids, antibiotics, immunosuppressives and surgery.
6. **Ophthalmic features**
   a. Uncommon. Acute anterior uveitis, conjunctivitis, episcleritis and peripheral corneal infiltrates.
   b. Rare. Retinal periphlebitis.

Fig. 20.25
Crohn disease involving the ileocaecal region

Cushing syndrome

Cushing syndrome is due to prolonged elevation of free plasma glucocorticoid levels.

1. **Causes**
   - Iatrogenic due to systemic administration of steroids (most common).
   - Hypersecretion of glucocorticoids by the adrenal cortex.
   - Hypersecretion of ACTH by a pituitary basophil adenoma (Cushing disease).
2. **Signs**
   a. Obesity may be generalized or classically involve the trunk, abdomen and neck (buffalo hump).

Fig. 20.28
Barium enema showing stricture and 'rose thorn' ulceration in Crohn disease (Courtesy of S. Ghiacy)

Fig. 20.29
Moon face, hyperpigmentation and hirsutism in Cushing syndrome

b. The face is swollen (moon face) and the complexion plethoric. Females may be hirsute (Fig. 20.29).

c. The skin is thin and susceptible to bruising. Purple striae may be seen (Fig. 20.30). Hyperpigmentation may develop with (ACTH-dependent) Cushing disease.

d. Other features include depression/psychosis, osteoporosis, poor wound healing and proximal myopathy.

3. **Complications** include hypertension, diabetes, pathological fractures and acute necrosis of the femoral head.
4. **Diagnostic tests** are targeted at first establishing the presence of elevated cortisol levels and then identifying the underlying cause (unless iatrogenic); they are best undertaken by an endocrinologist.

Fig. 20.30
Obesity and cutaneous striae in Cushing syndrome

5. **Treatment**
   a. Surgical removal of pituitary adenoma or adrenal secreting tumour. Ectopic foci of ACTH secretion may also be amenable to excision.
   b. Medical suppression of cortisol secretion with metyrapone or aminoglutethimide.
6. **Ophthalmic features**
   a. Common. Steroid-induced cataracts frequently develop in iatrogenic Cushing syndrome but not in Cushing disease.
   b. Uncommon. Bitemporal hemianopia is uncommon with secreting pituitary tumours, which tend to present with systemic features of hypersecretion, as opposed to non-secreting pituitary tumours, which tend to present with chiasmal compression. Glaucoma may develop in susceptible individuals with iatrogenic Cushing syndrome.

Diabetes mellitus

Diabetes mellitus is a common metabolic disorder characterized by sustained hyperglycaemia of varying severity secondary to lack, diminished efficacy, or both of endogenous insulin. The disease affects about 2% of the population in the UK. Despite some degree of overlap, diabetes can be divided into two types:

1. **Type 1** diabetes (insulin-dependent diabetes mellitus, IDDM, juvenile-onset diabetes) develops most frequently between the ages of 10 and 20 years, with acute symptoms of polydipsia, polyuria, nocturia and weight loss. There is an association with HLA-DR3 and -DR4. Autoimmune destruction of pancreatic islet cells is postulated as instrumental in pathogenesis. Type 1 diabetics are often lean and manifest a total lack of insulin; they may develop keto-acidosis and require insulin for glycaemic control.
2. **Type 2** diabetes (non-insulin-dependent diabetes mellitus, NIDDM, maturity-onset diabetes), on the other hand,

develops most frequently between the ages of 50 and 70 years. Type 2 diabetics are often overweight and manifest relative deficiency of insulin and/or peripheral insulin resistance. Metabolic control commonly involves diet and oral anti-diabetic drugs. Some patients may subsequently require insulin for glycaemic control, although many remain non-insulin-dependent. Type 2 diabetes is often initially asymptomatic, and discovered by chance. Alternatively, it may present with recurrent infections of the skin, vulva or glans penis or, rarely, with complications such as vitreous haemorrhage.

3. **Diagnostic tests**
   - A fasting glucose concentration of >6.7 mmol/l.
   - A random glucose concentration of >10.0 mmol/l.
   - A glucose tolerance test is performed only if the diagnosis is uncertain.
   - Glycosylated haemoglobin (HBA1c) reflects the average level of blood glucose over the preceding 6 weeks. Normally 4–8% of haemoglobin is glycosylated; values in excess of this reflect inadequacy of glycaemic control and is a better indicator of the efficacy or otherwise of treatment than a single random glucose level.
   - Urine testing for glycosuria is a crude and unsatisfactory means of monitoring diabetic control.

   NB: Glycosuria per se does not necessarily imply diabetes, as it may merely reflect a lowered renal threshold for glucose excretion.
4. **Treatment**. Type 1 diabetics require insulin; type 2 diabetics require a regimen involving weight reduction, physical exercise and diet control, often in combination with either or both oral hypoglycaemic agents and insulin. Oral anti-diabetic drugs include sulphonylureas (e.g. gliclazide, glipizide) and biguanides (e.g. metformin). It is also important to aggressively treat any associated problems, particularly hypertension and hyperlipidaemia.
5. **Systemic complications**
   a. *Renal*. Nephropathy is initially characterized by microscopic proteinuria. Severe renal disease may eventually result in renal failure requiring dialysis or transplantation.
   b. *Vascular*. Accelerated atherosclerosis of coronary and lower limb arteries. Severe involvement of legs may result in ischaemic ulceration and gangrene of the feet and toes (Fig. 20.31).
   c. *Neurological*
      - Sensory polyneuropathy principally affects the feet in a 'glove and stocking' distribution and may give rise to painless neuropathic perforating ulcers at pressure points in the soles (Fig. 20.32) and degenerative arthropathy (Charcot joints) (Fig. 20.33).
      - Cranial nerve palsies—classically the pupil-sparing third nerve palsy—may occur due to small vessel involvement.
   d. *Skin* manifestations include increased susceptibility to bacterial and fungal infections (Fig. 20.34), blistering of the feet and toes, necrobiosis lipoidica (Fig. 20.35) and lipodystrophy at sites of insulin injection (Fig. 20.36) and granuloma annulare.

Fig. 20.31
Diabetic gangrene

Fig. 20.32
Diabetic neuropathic ulceration

Fig. 20.33
Charcot joints

NB: Neuropathy in combination with vascular insufficiency and increased susceptibility to infection commonly results in gangrene of the extremities (diabetic foot).

Fig. 20.34
Moniliasis

Fig. 20.35
Necrobiosis lipoidica

Fig. 20.36
Diabetic lipodystrophy

6. **Ophthalmic features**
   a. *Common*. Retinopathy and iridopathy (increased Iris transillumination).
   b. *Uncommon*. Changes in refraction, accelerated senile cataract, rubeosis iridis, ocular motor nerve palsies and asteroid hyalosis.
   c. *Rare*. Papillopathy, pupillary light-near dissociation, acute-onset cataract and rhino-orbital mucormycosis.

Ehlers–Danlos syndrome type 6 (ocular sclerotic)

Ehlers–Danlos syndrome is a connective tissue disorder involving genetically determined abnormalities of collagen. There are 11 subtypes but only type 6 is associated with ocular features.

1. **Inheritance** is AR.
2. **Signs**
   a. *Skin*. Thinning, hyperelasticity (Fig. 20.37), bruising and slow healing.
   b. *Joints*. Hyperextensibility, easy dislocation, repeated falls, hydroarthrosis and pseudo-tumour formation over the knees and elbows.
   c. *Vascular*. Bleeding diathesis, dissecting aortic aneurysm, spontaneous rupture of large blood vessels and mitral valve prolapse.
3. **Ophthalmic features**
   a. *Common*. Ocular fragility with increased vulnerability to minimal trauma, blue sclera and microcornea.
   b. *Uncommon*. Ectopia lentis, keratoconus, cornea plana, high myopia, retinal detachment and angioid streaks.

Fig. 20.37
Cutaneous hyperelasticity in Ehlers–Danlos syndrome

Giant cell arteritis

Giant cell arteritis (GCA) is a granulomatous necrotizing arteritis (Fig. 20.38) with a predilection for large and medium-size arteries, particularly the superficial temporal, ophthalmic, posterior ciliary and proximal vertebral. The severity and extent of involvement are associated with the quantity of elastic tissue in the media and adventitia. Intracranial arteries, which possess little elastic tissue, are usually spared.

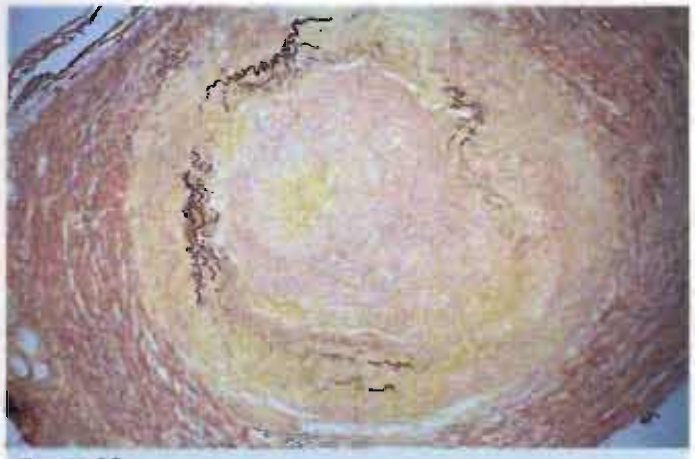

Fig. 20.38
Histology of giant cell arteritis showing granulomatous infiltration, disruption of the internal elastic lamina, proliferation of the intima and complete occlusion of the lumen (Courtesy of A. Garner)

Fig. 20.39
Dilated and tortuous superficial temporal artery in giant cell arteritis

Fig. 20.40
Scalp necrosis in giant cell arteritis

1. **Presentation** is usually in the seventh to eighth decades with the following:
   a. ***Scalp tenderness***, first noticed when combing the hair, is a frequent presenting complaint.
   b. ***Headache***, sometimes severe, may be localized to the frontal, occipital or temporal areas, or more generalized.
   c. ***Jaw claudication*** is virtually pathognomonic. It is caused by ischaemia of the masseter and causes pain on speaking and chewing.
   d. ***Polymyalgia rheumatica*** is characterized by pain and stiffness in proximal muscle groups (typically the shoulders). It is characteristically worse in the morning and after exertion and may precede cranial symptoms by many months.
   e. ***Non-specific symptoms*** such as neck pain, weight loss, fever, night sweats, malaise and depression are common.
   f. ***Blindness*** of sudden onset with minimal systemic upset (occult arteritis) is uncommon.
2. **Other features**
   a. ***Superficial temporal arteritis*** is characterized by thickened, tender, inflamed and nodular arteries (Fig. 20.39), which cannot be flattened against the skull. Pulsation is initially present, but later ceases, a sign strongly suggestive of GCA, since a non-pulsatile superficial temporal artery is highly unusual in a normal individual. In very severe cases, scalp gangrene may ensue (Fig. 20.40).

> ***NB:*** The best location to examine pulsation is directly in front of the pinna.

   b. ***Complications***. Dissecting aneurysms, aortic incompetence, myocardial infarction, renal failure and brain stem stroke.
3. **Diagnostic tests**
   a. ***Erythrocyte sedimentation rate*** (ESR) is often very high, with levels of >60 mm/h. In interpreting the ESR the following should be borne in mind:
      - The normal ESR equals roughly half the age in men; it is 5 mm higher in women.
      - ESR levels of 40 mm/h may be 'normal' in diabetics and in the elderly.
      - Approximately 20% of patients with GCA have a normal ESR.
   b. ***C-reactive protein*** is invariably raised and may be helpful when ESR is equivocal.
   c. ***Temporal artery biopsy*** (TAB) should be performed if GCA is suspected.
      - Steroids should never be withheld pending biopsy, which should ideally be performed within 3 days of commencing steroids.
      - Systemic steroids for more than 7 days may suppress histological evidence of active arteritis; however, this is not invariable and biopsy should still be performed even if steroid therapy has been commenced considerably earlier. This is for two reasons: firstly, if positive it justifies long-term administration of steroids in a population highly prone to their adverse effects. If negative, it provides some justification for tailing off and stopping steroid therapy.

- In patients with ocular involvement it is advisable to take the biopsy from the ipsilateral side. The ideal location is the temple because it avoids damage to a major branch of the auriculotemporal nerve.
- At least 2.5 cm of the artery should be taken and serial sections examined because of the phenomenon of 'skip lesions': segments of histologically normal arterial wall may alternate with segments of granulomatous inflammation.
- Lack of pulsation may render TAB difficult, especially in inexperienced hands; not uncommonly, a segment of nerve is excised and sent for histological examination.

4. **Treatment** involves the administration of systemic steroids (*see* Chapter 18).
5. **Ophthalmic features**
   a. Common. Anterior ischaemic optic neuropathy.
   b. Uncommon. Amaurosis fugax, cotton wool spots, central retinal artery occlusion, cilioretinal artery occlusion and ocular motor nerve palsies (commonly a pupil-sparing third nerve palsy).
   c. Rare. Ocular ischaemic syndrome.

Homocystinuria

Homocystinuria is caused by deficiency of cystathionine-β-synthetase leading to accumulation of homocystine and methionine. The condition is phenotypically similar to Marfan syndrome but carries a thrombotic tendency.

1. **Inheritance** is AR.
2. **Signs**
   - Blond hair with a malar flush (Fig. 20.41).
   - Marfanoid habitus but infrequent arachnodactyly.
   - Mental retardation and psychiatric disturbance.

Fig. 20.41
Blond hair and a malar flush in homocystinuria

3. **Complications**
   - Osteoporosis and spontaneous crush fractures.
   - Thromboses in any vessel and at any age, particularly postoperatively or postpartum.
4. **Treatment** involves oral pyridoxine to reduce homocystine and methionine levels.
5. **Ophthalmic features**
   a. Common. Ectopia lentis.
   b. Uncommon. Myopia and retinal detachment.

Hypertension

Hypertension is most commonly idiopathic (essential) and occasionally secondary to a renal or metabolic disorder.

1. **Presentation** is usually in the fifth to sixth decades.
2. **Signs.** Elevation of blood pressure >140/90 (although the degree of elevation required to diagnose hypertension varies with age).
3. **Complications**
   - Left ventricular hypertrophy and subsequent failure.
   - Increased risk of atherosclerosis resulting in coronary heart disease and stroke.
   - Renal disease.
4. **Treatment** options include lifestyle modification (exercise, weight reduction, diminished salt intake and alcohol consumption) and drug therapy (diuretics, beta-blockers, calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists and alpha-blockers).
5. **Ophthalmic features**
   a. Common. Retinal arteriolosclerosis and branch retinal vein occlusion.
   b. Uncommon. Retinopathy, retinal artery occlusion, retinal artery macroaneurysm, anterior ischaemic optic neuropathy, choroidal infarcts and ocular motor nerve palsies.
   c. Rare. Exudative retinal detachment (in eclampsia).

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is an inflammatory arthritis of at least 3 months duration developing in children before the age of 16 years. The female:male ratio is 3:2. Patients are seronegative for IgM rheumatoid factor. In North America, however, JIA is frequently referred to as juvenile 'rheumatoid' arthritis.

1. **Presentation.** Based on the onset and the extent of joint involvement during the first 6 months, three types of presentation are recognized:
   a. Pauciarticular-onset JIA accounts for about 60% of cases. It affects girls five times as often as boys, with a peak age of onset of around 2 years. The arthritis involves four or fewer joints, most commonly the knees (Fig. 20.42), although the ankles and wrists may also be affected. Some patients in this subgroup remain pauciarticular, while others subsequently develop a

Fig. 20.42
Pauciarticular juvenile idiopathic arthritis involving the knees

Fig. 20.43
Polyarticular juvenile idiopathic arthritis

polyarthritis. About 75% of children are positive for antinuclear antibodies (ANA).

- *Uveitis* is common in this group and affects about 20% of children. Risk factors for uveitis are early-onset of JIA, and positive findings for ANA and HLA-DR5.

b. ***Polyarticular***-onset JIA accounts for a further 20% of cases. It affects girls about three times as often as boys and may commence at any age throughout childhood. The arthritis involves five or more joints, with both small and large joints being involved symmetrically (Fig. 20.43). Systemic features are mild or absent. About 40% of children are positive for ANA.

- *Uveitis* occurs in about 5% of cases.

c. ***Systemic***-onset JIA accounts for about 20% of cases. The disease occurs with equal frequency in boys and girls and may occur at any age throughout childhood. Systemic features include a high remittent fever, transient maculopapular rash, generalized lymphadenopathy, hepatosplenomegaly and serositis. Initially, arthralgia or arthritis may be absent or minimal, and only a minority of patients subsequently develop a progressive polyarthritis. The term '*Still's disease*' is reserved for patients in this subgroup.

- *Uveitis* does not occur.

2. **Treatment** options include physiotherapy, NSAIDs and low-dose methotrexate.
3. **Ophthalmic features.** Chronic anterior uveitis.

Kearns–Sayre syndrome

Kearns–Sayre syndrome is a mitochondrial cytopathy associated with mitochondrial DNA deletions.

1. **Presentation** is in the first to second decades with an insidious onset of bilateral ptosis and limitation of ocular movements in all directions of gaze (progressive external ophthalmoplegia).
2. **Signs**
   - Ataxia and cardiac conduction defects.
   - Fatigue and proximal muscle weakness are common.
   - Deafness, diabetes, short stature and hypoparathyroidism may be present.

3. **Diagnostic tests.** Lumbar puncture shows increased CSF protein concentration (>1 g/l). ECG demonstrates cardiac conduction defects.
4. **Ophthalmic features.** Symmetrical ptosis, external ophthalmoplegia and pigmentary retinopathy.

Fig. 20.44
Lepromatous cutaneous plaques

Fig. 20.45
Lepromatous cutaneous nodules

Leprosy

Leprosy (Hansen disease, hanseniasis) is a chronic granulomatous infection caused by an intracellular acid-fast bacillus, *Mycobacterium leprae*. The exact mode of infection is unknown although the upper respiratory tract appears the most likely portal of entry.

1. **Lepromatous leprosy** is a generalized, multisystem infection with widespread lesions of skin, peripheral nerves, upper respiratory tract, reticuloendothelial system, eyes, bones and testes. Important signs include:
   a. Skin. Erythema nodosum, plaques (Fig. 20.44) and nodules (Fig. 20.45).

Fig. 20.46
Saddle-shaped nose in leprosy

Fig. 20.47
Shortening of digits in leprosy (Courtesy of T. Ffytche)

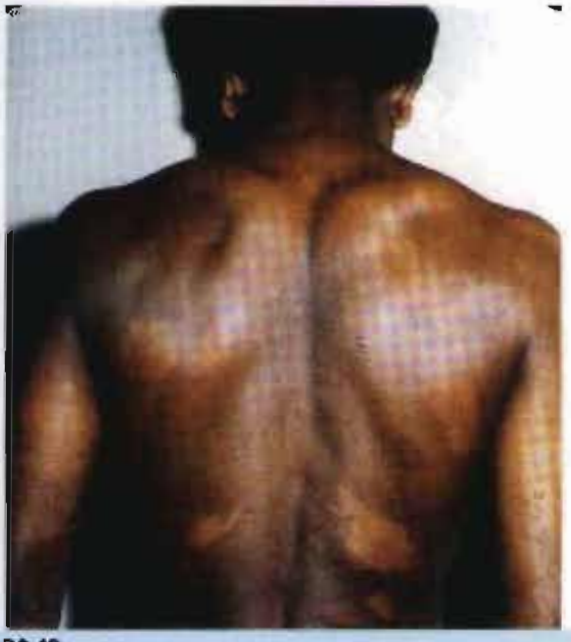

Fig. 20.48
Hypopigmented skin patches in leprosy

b. Nose. Mucosal thickening and saddle-shaped deformity (Fig. 20.46).

c. Neurological. Peripheral neuropathy results in loss of sensory, autonomic and motor function.

- Sensory neuropathy facilitates trauma which may result in shortening of digits (Fig. 20.47) from a multitude of mechanisms.
- Autonomic neuropathy leads to dry, cracked, infection-prone skin; often superimposed on this is secondary bacterial infection, with gross destruction of the tissues.
- Motor neuropathy is exemplified by the 'claw hand' deformity due to ulnar nerve palsy.

2. **Tuberculoid leprosy** is restricted to the skin and peripheral nerves.
   a. Skin. Annular, anaesthetic, hypopigmented lesions with raised edges (Fig. 20.48).
   b. Nerves. Thickening of cutaneous sensory nerves.
3. **Treatment** is with dapsone, rifampicin and clofazimine.
4. **Ophthalmic features**
   a. Common. Madarosis and lagophthalmos due to seventh nerve palsy. Neurotrophic keratitis due to trigeminal involvement.
   b. Uncommon. Anterior uveitis.

Lyme disease

Lyme disease (borreliosis) is an infection caused by a spirochete, *Borrelia burgdorferi*, transmitted through the bite of a deer tick, *Ixodes ricinus*. Systemic manifestations are complex and are best conceptualized as early and late.

1. **Early** stage presents several days after the bite with a pathognomonic annular expanding skin lesion (erythema chronicum migrans) which may be accompanied by constitutional symptoms and lymphadenopathy. This may last for several weeks and resolve even without treatment. Complications, both neurological (cranial nerve palsies, meningitis) and cardiac (conduction defects, myocarditis), may follow within 3–4 weeks of the initial manifestations.
2. **Late** complications, most commonly chronic arthritis of large joints, may ensue and cause problems for years. Polyneuropathy and chronic acrodermatitis may also occur.
3. **Diagnostic tests** include PCR and ELISA.
4. **Treatment** is with oral doxycycline or intravenous ceftriaxone for neurological involvement.
5. **Ophthalmic features**
   a. Common. Photophobia, pain, periocular oedema and conjunctivitis.
   b. Uncommon. Keratitis, anterior uveitis, intermediate uveitis, optic neuritis, neuroretinitis and ocular motor nerve palsies.
   c. Rare. Peripheral multifocal choroiditis and retinal periphlebitis.

Marfan syndrome

Marfan syndrome is a widespread disorder of connective tissue associated with mutation of the fibrillin gene on chromosome 15q.

1. **Inheritance** is AD with variable expressivity.

Fig. 20.49
Marfan syndrome (see text)

Fig. 20.50
Arachnodactyly in Marfan syndrome

2. Classical signs

a. Musculoskeletal

- Tall, thin stature, scoliosis, sternal deformity (prominence or depression).
- Disproportionately long limbs compared with the trunk (arm span > height) (Fig. 20.49).
- Long spider-like fingers (arachnodactyly) and mild joint hypermobility (Fig. 20.50).
- A narrow and high-arched (gothic) palate (Fig. 20.51).
- Muscular underdevelopment and predisposition to hernias.

b. Cardiovascular

- Dilatation of the ascending aorta leading to aortic incompetence and heart failure (Fig. 20.52).
- Mitral valve disease and aortic dissection.

c. Skin. Striae, fragility and easy bruising.

3. Ophthalmic features

a. Common. Ectopia lentis, hypoplasia of dilator pupillae, angle anomaly, myopia and retinal detachment.

b. Uncommon. Microspherophakia, keratoconus and cornea plana.

c. Rare. Megalocornea.

Fig. 20.51
High-arched palate in Marfan syndrome

Multiple sclerosis

Multiple sclerosis (MS) is an idiopathic, remitting, demyelinating disease involving white matter within the CNS.

1. Presentation is in the third to fourth decades with remitting/relapsing involvement occurring at random frequency and of unpredictable duration.

2. Signs

a. Spinal cord. Weakness, stiffness, sphincter disturbance and sensory loss with a 'trouser-like' distribution.

b. Brain stem. Diplopia, nystagmus, dysarthria and dysphagia.

c. Cerebral hemisphere. Hemiparesis, hemianopia and dysphasia.

d. Psychological. Intellectual decline, depression, euphoria and dementia.

3. Transient features include Lhermitte sign (electrical sensation on neck flexion), dysarthria–dysequilibrium–diplopia syndrome and Uhthoff phenomenon (sudden worsening of vision or other symptoms on exercise or increase in body temperature).

4. Diagnostic tests

a. Lumbar puncture shows leucocytosis, IgG level > 15% of total protein and oligoclonal bands on protein electrophoresis.

b. MRI shows ovoid periventricular and corpus callosum plaques with their long axes perpendicular to the ventricular margins (*see* Figs 18.24 and 18.25). Acute demyelination plaques may be highlighted with gadolinium on T1-weighted scans.

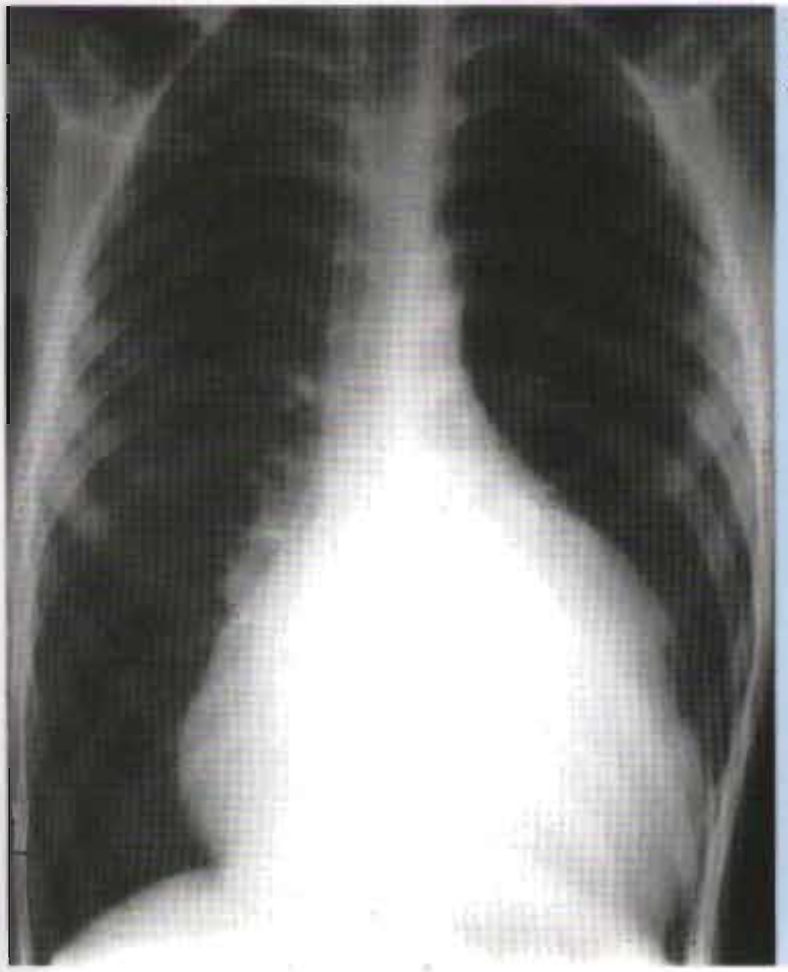

Fig. 20.52
Elongated chest and enlarged heart in Marfan syndrome
(Courtesy of S. Ghiacy)

5. **Treatment** options include systemic steroids and interferon beta-1a.
6. **Ophthalmic features**
   a. *Common*. Optic neuritis (usually retrobulbar), internuclear ophthalmoplegia and nystagmus.
   b. *Uncommon*. Skew deviation, ocular motor nerve palsies and hemianopia.
   c. *Rare*. Intermediate uveitis and retinal periphlebitis.

Myasthenia gravis

Myasthenia gravis is an autoimmune disease in which antibodies mediate damage and destruction of acetylcholine receptors in striated muscle. The resultant impairment of neuromuscular conduction causes weakness and fatiguability of skeletal musculature but not of cardiac and involuntary muscles. The disease affects females twice as commonly as males. Myasthenia may be (a) *ocular*, (b) *bulbar* or (c) *generalized*.

1. **Presentation** is most commonly in the third decade, but may be at any time after the first year of life, most frequently with ptosis or diplopia. Patients with generalized involvement then develop painless fatigue often brought on by exercise, which may be worse towards the end of the day and provoked by infection or stress.
2. **Signs.** The most important feature is fatiguability, affecting musculature of the limbs and that involved in facial expression, ocular movements, mastication and speech.
   a. *Peripheral*. Weakness, particularly of the arms and proximal muscles of the legs. Permanent myopathic wasting may occur in long-standing cases.
   b. *Facial*. Lack of expression (myopathic facies) and ptosis.
   c. *Bulbar*. Difficulties with swallowing (dysphagia), speaking (dysarthria) and chewing.
   d. *Respiratory*. Difficulty with breathing is rare but serious.
3. **Diagnostic tests**
   - Positive edrophonium test (*see* Chapter 18).
   - Raised serum acetylcholine receptor antibody levels.
   - Thoracic CT (Fig. 20.53) or MRI to detect thymoma which is present in 10% of patients. Patients under the age of 40 years without thymoma generally have a hyperplastic thymus; in older patients the thymus is usually normal (atrophic).
4. **Treatment** options include anticholinesterase drugs (pyridostigmine, neostigmine), steroids, immunosuppressive drugs (azathioprine, cyclosporin), plasma exchange, intravenous immunoglobulins and thymectomy. Patients with pure ocular myasthenia are usually not helped by thymectomy.
5. **Ophthalmic features**
   a. *Common*. Ptosis and diplopia. Inability to maintain upgaze. Cogan 'lid-twitch' sign. Weakness of orbicularis oculi with compromised lid closure.
   b. *Uncommon*. Pseudo-internuclear ophthalmoplegia.

Fig. 20.53
CT scan of the mediastinum showing a thymoma

NB: Bizarre defects of ocular motility may occur; myasthenia should therefore be considered in the differential diagnosis of any ocular motility disorder that does not fit with a recognized pattern.

Myotonic dystrophy

Myotonic dystrophy (dystrophia myotonica, Steinert disease) is characterized by delayed muscular relaxation after cessation of voluntary effort (myotonia). The gene locus is on 19q13.3.

1. **Inheritance** is AD.
2. **Presentation** is in the third to sixth decades with weakness of the hands and difficulty in walking. Successive generations exhibit progressively earlier onset and greater severity of disease, a phenomenon termed 'anticipation'.
3. **Signs**
   a. *Peripheral.* Difficulty in releasing grip (Fig. 20.54), muscle wasting and weakness.
   b. *Central.* Mournful facial expression (Fig. 20.55) caused by bilateral facial wasting with hollow cheeks and slurred speech from involvement of the tongue and pharyngeal muscles.
   c. *Other.* Frontal baldness in males (Fig. 20.56), hypogonadism, mild endocrine abnormalities, cardiomyopathy, pulmonary disease, intellectual deterioration and bone changes.
4. **Diagnostic tests.** Electromyography shows myotonic and myopathic potentials, and serum creatine kinase is elevated.

Fig. 20.54
Difficulty in relaxation of grip in myotonic dystrophy

5. **Treatment** involves exercise and prevention of contractures.
6. **Ophthalmic features**
   a. *Common.* Early-onset stellate cataracts and ptosis.
   b. *Uncommon.* External ophthalmoplegia, pupillary light-near dissociation, mild pigmentary retinopathy and low intraocular pressure.

Neurofibromatosis-1

Neurofibromatosis-1 (NF-1, von Recklinghausen disease) is a phacomatosis that primarily affects cell growth of neural tissues. The gene locus is on 17q11.

Fig. 20.55
Mournful facial expression in myotonic dystrophy

Fig. 20.56
Mournful facial expression, frontal balding and right cataract in myotonic dystrophy

Fig. 20.57
Mild macrocephaly in NF-1

Fig. 20.58
Right facial hemiatrophy and fibroma mollusca in NF-1

1. **Inheritance** is AD with irregular penetrance and variable expressivity.
2. **Signs**
   a. ***Neural tumours*** in the CNS and in cranial, peripheral and sympathetic nerves.
   b. ***Skeletal.*** Short stature, mild macrocephaly (enlarged head) (Fig. 20.57), facial hemiatrophy (Fig. 20.58), absence of the great wing of the sphenoid bone (*see* Fig. 18.117), scoliosis and thinning of long bone cortex.
   c. ***Skin***
      - Café-au-lait spots are flat, light-brown patches (Figs 20.59c and 20.60). They appear during the first year of life and increase in size and number throughout childhood; teenagers and adults invariably have more than six.
      - Axillary freckles usually become obvious around the age of 10 years and are pathognomonic.
      - Fibroma mollusca are pedunculated, flabby nodules (Fig. 20.61) which are often widely distributed over the body (Fig. 20.62 and *see* Fig. 20.59b). They appear at about puberty and increase in number throughout life.

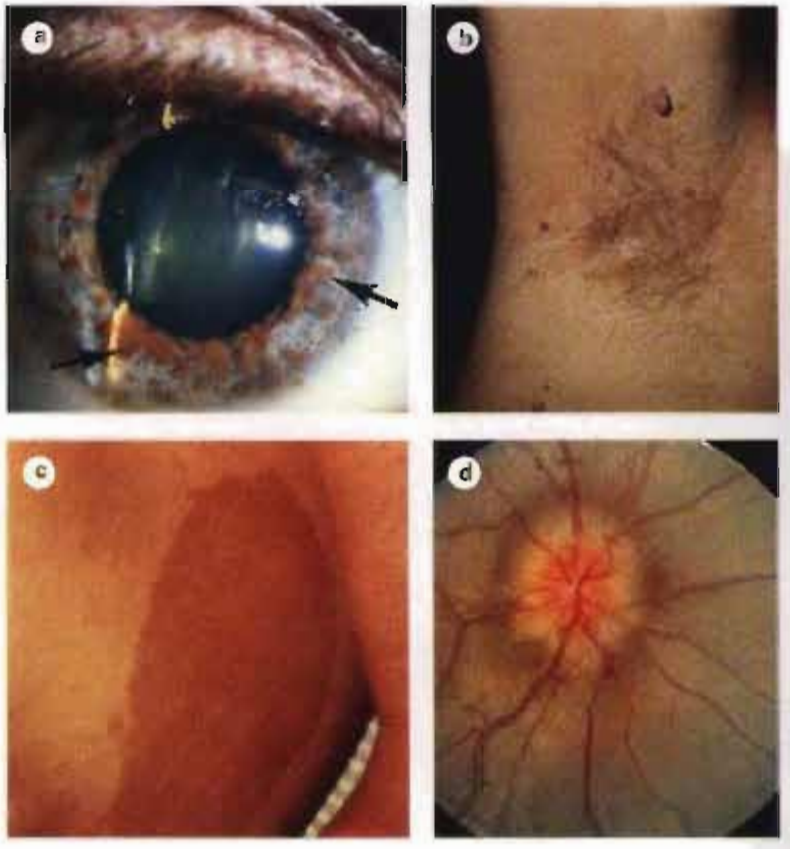

Fig. 20.59
NF-1. (a) Lisch nodules; (b) fibroma mollusca; (c) café-au-lait spot; (d) optic disc oedema due to optic nerve glioma (Courtesy of Wilmer Institute)

Fig. 20.60
Café-au-lait spots in NF-1

Fig. 20.61
Fibroma mollusca in NF-1

- Plexiform neurofibromas may be associated with pigmentation and overgrowth of the overlying soft tissues (Fig. 20.63 and Fig. 20.64). They may be present at birth or appear during childhood and may occur anywhere on the body. Rarely they may involve the face and cause disfigurement (Fig. 20.65).

3. **Associations** include malignancies, hypertension and mental handicap.
4. **Ophthalmic features**
   a. ***Common.*** Eyelid neurofibromas and Lisch nodules (*see* Fig. 20.59a).
   b. ***Uncommon.*** Optic nerve glioma (*see* Fig. 20.59d), ectropion uveae and glaucoma.
   c. ***Rare.*** Other neural orbital tumours, spheno-orbital encephalocele, prominent corneal nerves, iris mammillations, choroidal naevi, choroidal melanomas and retinal astrocytomas.

Neurofibromatosis-2

Neurofibromatosis-2 (NF-2) is less common than NF-1, with the gene locus at 22q12.

Fig. 20.62
Extensive fibroma mollusca in NF-1

Fig. 20.63
Plexiform fibroma of the right palm in NF-1

Fig. 20.64
Plexiform neurofibroma and soft tissue hypertrophy in NF-1

Fig. 20.65
Extensive facial plexiform neurofibroma and soft tissue hypertrophy in NF-1

1. **Inheritance** is AD.
2. **Diagnostic criteria**
   a. ***Bilateral acoustic neuromas*** which usually present in the late teens or early twenties with hearing loss, tinnitus or imbalance. Most acoustic neuromas are schwannomas arising from the vestibular nerve. In young patients tumour growth is invariably fast, whereas in older patients the lesion may be either slow- or fast-growing. Recent advances in microsurgical techniques have significantly improved the results of surgery. The gamma-knife (stereotactic radiotherapy) provides a therapeutic option.
   b. ***A patient with a first-degree relative with NF-2*** who also has either a unilateral acoustic neuroma or two of the following: neurofibroma, meningioma, glioma, schwannoma or juvenile cataract.
3. **Ophthalmic features**
   a. ***Common.*** Early-onset cataract.
   b. ***Uncommon.*** Ophthalmoplegia, combined hamartomas of the RPE and retina and epiretinal membranes.

Polyarteritis nodosa

Polyarteritis nodosa (PAN) is an idiopathic, potentially lethal, collagen vascular disease affecting medium-sized and small arteries, with frequent aneurysm formation. It is three times more common in males than in females.

1. **Presentation** is in the third to sixth decades with tachycardia, myalgia, arthralgia, fever and weight loss.

Fig. 20.66
Cutaneous vasculitis

Fig. 20.67
Skin papules in pseudoxanthoma elasticum

2. **Signs**
   a. Skin. Purpura and easy bruising, vasculitis (Fig. 20.66), infarcts, gangrene and livedo reticularis.
   b. Muscles. Weakness and tenderness.
3. **Complications**
   - Renal involvement and hypertension.
   - Coronary arteritis which may lead to heart failure and myocardial infarction.
   - Gastrointestinal bleeding or an acute abdominal crisis.
   - Stroke or multifocal neuropathy.
4. **Diagnostic tests** show eosinophilia, hypergammaglobulinaemia and necrotizing lesions on skin biopsy.
5. **Treatment** is with systemic steroids and immunosuppressive agents.
6. **Ophthalmic features**
   a. Common. Peripheral ulcerative keratitis and scleritis.
   b. Rare. Orbital pseudo-tumour and occlusive retinal periarteritis.

Fig. 20.68
Loose axillary skin in pseudoxanthoma elasticum

Pseudoxanthoma elasticum

Pseudoxanthoma elasticum is a hereditary disorder of elastin. There are four distinctive types, in which ocular manifestations are common but of variable severity.

1. **Dominant type 1**
   - Small, yellowish skin papules arranged in linear or reticulate plaques most commonly on the neck (Fig. 20.67), axillae (Fig. 20.68), antecubital fossae, groins and paraumbilical area (Fig. 20.69). involved skin becomes progressively loose.
   - Thin, delicate skin which bruises easily.
   - Accelerated atherosclerosis and mitral valve disease.
   - Severe angioid streaks (Groenblad–Strandberg syndrome).
2. **Dominant type 2**
   - Fewer and flatter skin papules than in dominant type 1.
   - Skin hyperelasticity and high-arched palate.
   - Mild angioid streaks and blue sclera.
3. **Recessive type 1**
   - Skin changes are similar to dominant type 1.

Fig. 20.69
Pseudoxanthoma elasticum involving the paraumbilical area

- Mild vascular disease but frequent gastrointestinal bleeding.
- Mild angioid streaks.

4. **Recessive type 2**
   - Severe and generalized skin changes.
   - No systemic complications.
   - Angioid streaks.

Psoriatic arthritis

Psoriatic arthritis is a spondarthropathy which develops in about 7% of patients with psoriasis. The disease affects both sexes equally and is associated with an increased prevalence of HLA-B27 and HLA-B17.

1. **Presentation** is in the third to fourth decades.
2. **Signs**
   a. Skin
   - Plaque psoriasis (most common): well-demarcated, salmon-pink areas covered with thick, silvery plaques, commonly seen on extensor surfaces and the scalp (Fig. 20.70).
   - Flexural psoriasis: non-scaly pink lesions, commonly affecting the groin and perineum.
   - Pustular psoriasis is characterized by pustular lesions on the palms and soles in association with scaling and erythema.
   - Erythrodermic psoriasis is characterized by severe erythema and scaling, often with pustule formation, involving the trunk and limbs.

   b. Arthritis may take one of the following patterns:
   - Asymmetrical involvement of the distal interphalangeal joints which may give rise to sausage-shaped deformities (Fig. 20.71).
   - Pauciarticular peripheral involvement.
   - Symmetrical peripheral involvement similar to rheumatoid arthritis.
   - Arthritis mutilans affecting a few digits is rare.
   - Associated ankylosing spondylitis.

   c. Nail dystrophy. Pitting, transverse depression and onycholysis (Fig. 20.72).

Fig. 20.70

Fig. 20.71
Sausage-like deformities of digits in psoriatic arthritis

Fig. 20.72
Psoriatic nail dystrophy

3. **Treatment**. NSAIDs, intra-articular steroids; severe disease may require cytotoxic drugs.
4. **Ophthalmic features**
   a. Uncommon. Acute anterior uveitis.
   b. Rare. Conjunctivitis, keratitis and keratoconjunctivitis sicca.

Reiter syndrome

Reiter syndrome (reactive arthritis) is a spondarthropathy which typically affects young males and is characterized by the triad of urethritis, conjunctivitis and arthritis. About 70% of patients are positive for HLA-B27.

1. **Presentation** is in the third to fourth decades with urethritis, conjunctivitis and arthritis, occurring within a short period of each other, classically following dysentery or sexual intercourse. Presentation may, however, be insidious.
2. **Signs**
   a. Arthritis. Asymmetrical involvement of the knees or ankles is most common and may be migratory. The shoulders, wrists, elbows, hips, spine and sacro-iliac

Fig. 20.73
Achilles tenosynovitis in Reiter syndrome

Fig. 20.74
Keratoderma blenorrhagica in Reiter syndrome

Fig. 20.75
Circinate balanitis and urethral discharge in Reiter syndrome

*b. **Enthesopathy**.* Plantar fasciitis, Achilles tendonitis (Fig. 20.73), bursitis and calcaneal periostitis. Reactive bone formation in the latter may result in a calcaneal spur.

*c. **Mucocutaneous**.* Painless mouth ulceration, keratoderma blenorrhagica involving the palms and soles (Fig. 20.74), circinate balanitis (Fig. 20.75) and nail dystrophy.

*d. **Genitourinary**.* Cystitis, cervicitis, prostatitis, epididymitis and orchitis.

*e. **Aortic incompetence*** is uncommon.

3. **Treatment** is with NSAIDs.
4. **Ophthalmic features**
   *a. **Common**.* Conjunctivitis and acute anterior uveitis.
   *b. **Uncommon**.* Corneal infiltrates.

Rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune systemic disease characterized by a symmetrical, destructive, deforming, inflammatory polyarthropathy, in association with a spectrum of extra-articular manifestations and circulating antiglobulin antibodies, termed rheumatoid factors. It affects females more commonly than males.

1. **Presentation** is in the fourth decade and occasionally in childhood (juvenile rheumatoid arthritis). The disease is characterized by exacerbations alternating with phases of quiescence.
2. **Signs**
   a. Arthritis
   - Symmetrical involvement of the small joints of the hands and feet, inflammation typically involves the proximal interphalangeal and spares the distal interphalangeal joints. The metacarpophalangeal and wrist joints are also commonly involved.
   - Less frequent involvement of the shoulders, elbows, hips and cervical spine.
   - Joint instability secondary to chronic inflammation may result in subluxation and deformities, such as ulnar deviation of the metacarpophalangeal joints (Fig. 20.76).

   b. Skin. Raynaud phenomenon, vasculitis (Fig. 20.77), subcutaneous nodules (Fig. 20.78) and occasionally pyoderma gangrenosum.

Fig. 20.76
Ulnar deformity of the right hand in rheumatoid arthritis

Fig. 20.77
Cutaneous vasculitis in rheumatoid arthritis

Fig. 20.78
Rheumatoid nodules

Fig. 20.79
Acne rosacea—stage 1 (see text)

Fig. 20.80
Severe acne rosacea—stage 2 (see text)

3. **Complications**
   - Pulmonary nodules and fibrosis.
   - Multifocal neuropathy.
   - Septic arthritis.
   - Secondary amyloidosis.
   - Carpal tunnel syndrome.
4. **Treatment** options include NSAIDs, gold salts, D-penicillamine, hydroxychloroquine, sulphasalazine, steroids and cytotoxic agents.
5. **Ophthalmic features**
   a. Common. Keratoconjunctivitis sicca (secondary Sjögren syndrome).
   b. Uncommon. Scleritis and peripheral ulcerative keratitis.
   c. Rare. Acquired superior oblique tendon sheath syndrome.

Rosacea

Rosacea is an idiopathic skin disease which principally affects the glabella, cheeks, nose and chin.

1. **Presentation** is in adult life with itching and flushing of facial skin, often precipitated by alcohol or spicy food.
2. **Signs**
   - *Stage 1.* Erythema progressing to telangiectasia (Fig. 20.79).
   - *Stage 2.* Papules and pustules (Fig. 20.80).
   - *Stage 3.* Inflammatory nodules, sebaceous gland hyperplasia (Fig. 20.81) and rhinophyma.
3. **Treatment** is with topical metronidazole gel and systemic tetracycline.
4. **Ophthalmic features**
   a. Common. Chronic posterior blepharitis and recurrent meibomian cysts.
   b. Uncommon. Conjunctivitis and peripheral keratitis.

Sarcoidosis

Sarcoidosis is an idiopathic multi-system granulomatous inflammatory disorder, more common in patients of African descent than in Caucasians.

1. **Presentation**
   a. Acute-onset sarcoidosis typically occurs during the third decade:
   - Löfgren syndrome is characterized by fever, erythema nodosum (Fig. 20.82), bilateral hilar lymphadenopathy (Fig. 20.83) and frequently arthralgia.

Fig. 20.81
Acne rosacea—stage 3 (see *text*)

Fig. 20.82
Erythema nodosum

Fig. 20.83
Bilateral hilar lymphadenopathy in acute sarcoidosis

Fig. 20.84
Facial palsy and lupus pernio involving the nose in sarcoidosis

- Heerfordt syndrome (uveoparotid fever) is characterized by fever, parotid gland enlargement and uveitis.
- Seventh nerve palsy (Fig. 20.84) may be associated with other neurological features.

b. Insidious-onset sarcoidosis typically occurs during the fifth decade with fatigue, dyspnoea and arthralgia.

2. Signs

a. Pulmonary involvement is present in 90% of patients and varies in severity from asymptomatic bilateral hilar lymphadenopathy to progressive pulmonary fibrosis and bronchiectasis.

b. Skin. Erythema nodosum, granulomata (Fig. 20.85) and lupus pernio (Fig. 20.86). The latter is characterized by indurated, purple-blue lesions.

c. Neurological. Cranial nerve palsies (particularly facial), meningeal infiltration, and intracranial and intraspinal granulomas.

d. Other. Reticuloendothelial, hepatic, renal, bone and cardiac involvement.

3. Diagnostic tests

a. Chest radiographs are abnormal in 90% of cases.

b. Biopsy

- Of the lungs gives the greatest yield (90%).
- Of the conjunctiva is positive in about 70% of patients.
- Of lacrimal glands is positive in 25% of unenlarged and 75% of enlarged glands.

Fig. 20.85
Cutaneous sarcoid granulomas

Fig. 20.86
Lupus pernio

*c. **Serum angiotensin-converting enzyme*** (ACE) is elevated in patients with active disease but normal during remissions. The normal serum level in adults is 32.1 ± 8.5 IU. In patients with suspected neurosarcoid ACE can be measured in the cerebrospinal fluid. ACE may also be elevated in other conditions such as tuberculosis, lymphoma and asbestosis.

*d. **Bronchioalveolar lavage*** shows a raised proportion of activated T-helper lymphocytes.

*e. **Calcium assay*** may be useful because calcium metabolism is abnormal. Hypercalciuria is common but hypercalcaemia is unusual.

*f. **Gallium-67 scanning*** of the head, neck and thorax frequently shows increased uptake.

*g. **Pulmonary function tests*** reveal a restrictive lung defect with reduced total lung capacity.

4. **Treatment** options include NSAIDs, steroids and low-dose cytotoxic agents.
5. **Ophthalmic features**
   *a. **Common.*** Conjunctival granulomas, anterior uveitis, posterior uveitis and retinal periphlebitis.
   *b. **Uncommon.*** Keratoconjunctivitis sicca and intermediate uveitis.
   *c. **Rare.*** Fundus granulomas, retinal and disc neovascularization, and papilloedema.

Sjögren syndrome

Sjögren syndrome is characterized by autoimmune inflammation and destruction of lacrimal and salivary glands. The condition is classified as primary when it exists in isolation, and secondary when associated with other diseases such as rheumatoid arthritis and systemic lupus erythematosus. Primary Sjögren syndrome affects females more commonly than males.

1. **Presentation** is in adult life with grittiness of the eyes and dryness of the mouth.
2. **Signs**
   - Enlargement of the salivary glands with diminished salivary flow rate and a dry fissured tongue (Fig. 20.87).
   - Dry nasal passages, diminished vaginal secretions and dyspareunia.
   - Raynaud phenomenon and cutaneous vasculitis.
3. **Complications**
   - Reflux oesophagitis and gastritis.
   - Malabsorption due to pancreatic failure.
   - Pulmonary disease, renal disease and polyneuropathy.
4. **Diagnostic tests.** Serum autoantibodies, Schirmer test and biopsy of minor salivary glands.
5. **Treatment** options include systemic steroids and cytotoxic agents.
6. **Ophthalmic features**
   *a. **Common.*** Keratoconjunctivitis sicca.
   *b. **Rare.*** Adie pupil.

Fig. 20.87
Dry fissured tongue in Sjögren syndrome

Stevens–Johnson syndrome

Stevens–Johnson syndrome (erythema multiforme major) is an acute, serious but generally self-limiting mucocutaneous, blistering disease, primarily occurring in healthy young individuals. The most frequent precipitating factors of this severe type III hypersensitivity reaction are certain drugs (e.g. sulphonamides, tetracycline, NSAIDs and penicillin), infections with *Mycoplasma pneumoniae* and herpes simplex, and radiotherapy for malignancy. In over 50% of cases there is no apparent cause. The underlying pathology is a generalized vasculitis secondary to deposition of circulating immune complexes.

1. **Presentation** is in the third to fifth decades with constitutional symptoms followed by mucocutaneous lesions.
2. **Signs**
   a. Mucosa
   - Oral and nasal blisters, which rupture forming erosions, are universal; the lips exhibit haemorrhagic crusting (Fig. 20.88).
   - Genital involvement may occur (Fig. 20.89).

Fig. 20.88
Haemorrhagic crusting in Stevens–Johnson syndrome

Fig. 20.89
Involvement of the glans penis in Stevens–Johnson syndrome

   b. Skin
   - A generalized erythematous papular rash, which evolves into 'target' lesions, consisting of erythematous centres surrounded by pale areas, in turn encircled by erythematous rings (Fig. 20.90).
   - Blisters are usually transient but may be widespread and associated with haemorrhage and necrosis (Fig. 20.91).
   - Healing occurs within 1–4 weeks, sometimes leaving a scar.
3. **Treatment** is with systemic steroids; aciclovir may be used if herpes simplex is suspected as the causative agent.
4. **Ophthalmic features**
   a. Common. Transient membranous conjunctivitis.
   b. Uncommon. Cicatricial conjunctivitis.

Sturge–Weber syndrome

Sturge–Weber syndrome (encephalotrigeminal angiomatosis) is a sporadic phacomatosis.

Fig. 20.90
Target lesion in Stevens–Johnson syndrome

Fig. 20.91
Haemorrhagic vesiculobullous skin lesions and area of necrosis in Stevens–Johnson syndrome

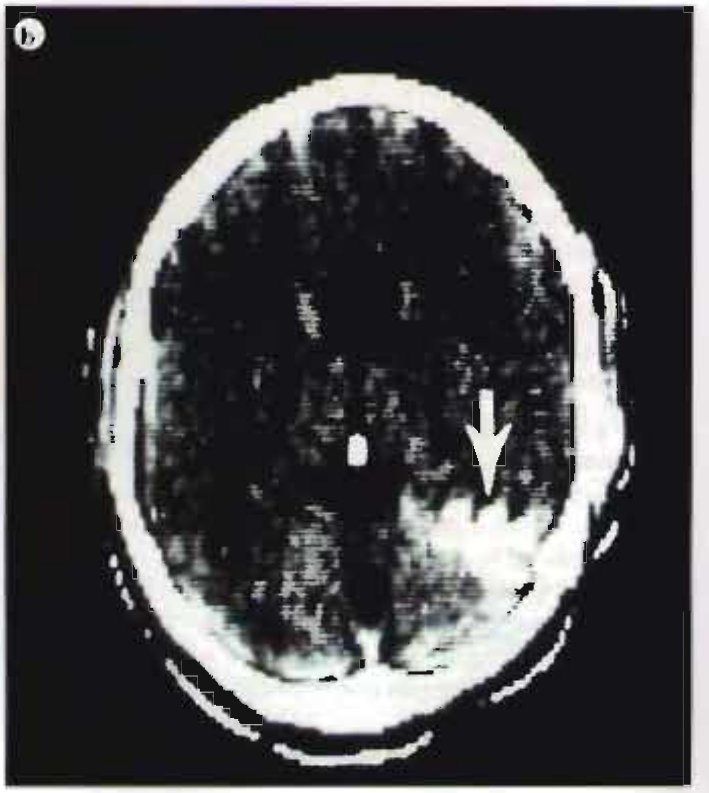

Fig. 20.92
Sturge–Weber syndrome. (a) Naevus flammeus; (b) axial CT scan showing a meningeal haemangioma (Courtesy of Wilmer Institute)

1. **Classification**
   - *a. Trisystem* involves the face, leptomeninges and eyes.
   - *b. Bisystem* involves the face and eyes or the face and leptomeninges.
2. **Presentation** is at birth.
3. **Signs**
   - Facial naevus flammeus (port-wine stain), extending over an area corresponding to the distribution of one or more branches of the trigeminal nerve (Fig. 20.92a).
   - Ipsilateral parietal or occipital leptomeningeal haemangioma may cause contralateral focal or generalized seizures, hemiparesis and hemianopia.
   - Mental retardation is frequent.
4. **Diagnostic tests.** Plain radiographs may show 'tramline markings' of cerebral calcification. The haemangioma will also be apparent on CT (Fig. 20.92b) and MRI.
5. **Ophthalmic features**
   - *a. Common.* ipsilateral glaucoma and diffuse choroidal haemangioma.
   - *b. Uncommon.* Ipsilateral episcleral haemangioma.
   - *c. Rare.* Heterochromia iridis.

Syphilis: acquired

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*.

1. **Stages**
   - *a. Primary* stage occurs after an incubation period commonly lasting 2–4 weeks and is characterized by a painless ulcer (chancre) at the site of inoculation (usually genitalia) and associated regional lymphadenopathy.
   - *b. Secondary* stage usually occurs 6–8 weeks after the chancre and is characterized by:
     - Generalized lymphadenopathy with mild or absent constitutional symptoms.

Fig. 20.93
Rash in secondary syphilis

Fig. 20.94
Rash in secondary syphilis

- Symmetrical maculopapular rash on the trunk (Fig. 20.93), palms and soles (Fig. 20.94).
- Condylomata lata in the anal region.
- Mucous patches in the mouth, pharynx and genitalia consisting of painless greyish-white circular erosions ('snail-track ulcers').
- Meningitis, nephritis and hepatitis may occur.
- Secondary syphilis resolves in a few months, even without treatment.

c. Latent stage follows resolution of secondary syphilis, may last for years and can be detected only by serological tests.

d. Tertiary stage occurs in about 40% of untreated cases and is characterized by:

- Cardiovascular manifestations: aortitis with aneurysm formation and aortic regurgitation.
- Neurosyphilis: tabes dorsalis, Charcot joints and general paralysis of the insane.
- Gummata in various organs.

2. Diagnostic tests

a. VDRL (Venereal Disease Research Laboratory). The titres reflect disease activity. It becomes positive during the primary stage and may become negative if treatment is given early.

b. FTA-ABS (fluorescent treponemal antibody absorption) is specific for treponema antibodies but is not titratable.

c. MHA-TP (microhaemagglutination assay with *Treponema pallidum* antigen) is specific for treponema antibodies but may be negative in early primary syphilis.

3. Treatment may be with procaine penicillin, doxycycline or erythromycin.

4. Ophthalmic features

a. Common. Madarosis and keratitis.

b. Uncommon. Anterior uveitis, chorioretinitis, periarteritis and neuroretinitis.

c. Rare. Optic neuritis, Argyll Robertson pupils and ocular motor nerve palsies.

Syphilis: congenital

Transplacentally acquired infection may result in stillbirth, stigmata of congenital syphilis or be subclinical.

1. Signs

a. Early

- Rhinitis and failure to thrive.
- Maculopapular rash, especially on the buttocks and thighs, and mucosal ulcers.
- Fissures around the lips, nares and anus.
- Pneumonia, hepatosplenomegaly, lymphadenopathy and jaundice.

b. Late

- Sensorineural deafness.
- Frontal bossing, short maxilla, prognathism, high-arched palate and saddle-shaped nose.
- Malformed incisors (Hutchinson teeth) and mulberry molars.

2. Ophthalmic features

a. Common. Anterior uveitis and interstitial keratitis in early cases.

b. Uncommon. Pigmentary retinopathy in late cases.

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is an autoimmune, non-organ-specific connective tissue disease characterized by numerous autoantibodies and circulating immune complexes, which mediate widespread vasculitis and tissue damage. It predominantly affects young females.

1. Presentation is in the third to fifth decades with fatiguability without specific organ involvement. Alternatively, the disease may present with symmetrical arthralgia.

2. Signs

a. Mucocutaneous. 'Butterfly' facial rash (Fig. 20.95), discoid rash (Fig. 20.96), vasculitis, telangiectasia, photosensitivity, alopecia, oral ulceration and Raynaud phenomenon.

b. Musculoskeletal. Arthritis, myositis and tendonitis.

c. Renal. Glomerulonephritis.

d. Cardiovascular. Pericarditis, endocarditis, myocarditis, and arterial and venous occlusions.

e. Pulmonary. Pleurisy, atelectasis and 'shrinking lungs'.

f. Haemopoietic. Anaemia, thrombocytopenia, lymphopenia and leucopenia.

g. Reticuloendothelial. Splenomegaly and lymphadenopathy.

h. Neurological. Polyneuritis, cranial nerve palsies, spinal cord lesions, epilepsy, stroke and psychosis.

3. Diagnostic tests

- The ESR is raised, but C-reactive protein is usually not.

Fig. 20.95
'Butterfly' rash in systemic lupus erythematosus

Fig. 20.96
Discoid lupus

- A variety of autoantibodies including lupus anticoagulant, antiphospholipid and antinuclear may be present.

4. **Treatment** options include antimalarials, NSAIDs, steroids and cytotoxic agents.
5. **Ophthalmic features**
   - *a. Common*. Madarosis and keratoconjunctivitis sicca.
   - *b. Uncommon*. Peripheral ulcerative keratitis.
   - *c. Rare*. Scleritis, retinal vasculitis and optic neuropathy.

Systemic sclerosis

Systemic sclerosis is an idiopathic, chronic, connective tissue disease affecting the skin (scleroderma) and internal organs, occurring most commonly in females under the age of 50. The risk of internal organ involvement is proportional to the extent of skin involvement. Systemic sclerosis may be (a) *limited*, (b) *diffuse*, (c) *sine scleroderma* and (d) *overlap* with other autoimmune diseases.

1. **Presentation** is in the fourth to sixth decades with Raynaud phenomenon.
2. **Signs**
   - *a. Skin*
     - Tightening and thickening on hands, feet, face and trunk (Fig. 20.97) gives rise to a waxy appearance.
     - Subcutaneous fibrosis causes binding-down of skin, tapering of the fingers with loss of pulps (sclerodactyly) (Fig. 20.98) and subcutaneous deposition of calcium (calcinosis).
     - A typical facial appearance characterized by a fixed expression, restrictive movements of the lips and 'beaking' of the nose often develops.
   - *b. Organs*
     - Oesophageal dysmobility.
     - Heart, lung and kidney disease.
     - Mild arthritis and myositis.
3. **Diagnostic tests**. Positive serum antinuclear and other autoantibodies; skin biopsy.
4. **Treatment** is unsatisfactory.
5. **Ophthalmic features**
   - *a. Common*. Eyelid tightening and telangiectasia.
   - *b. Uncommon*. Keratoconjunctivitis sicca.

Fig. 20.97
Scleroderma involving abdominal skin

Fig. 20.98
Sclerodactyly

Fig. 20.99
Goitre in hyperthyroidism

c. Rare. Conjunctival forniceal shortening and vascular changes, nodular episcleritis, scleral pits, retinal cotton wool spots and patches of choroidal non-perfusion seen only on fluorescein angiography.

Thyrotoxicosis

Thyrotoxicosis (hyperthyroidism) is a clinical condition involving excessive secretion of thyroid hormones. Graves disease, the most common subtype of hyperthyroidism, is an autoimmune disorder in which IgG antibodies bind to thyroid-stimulating hormone (TSH) receptors in the thyroid gland and stimulate secretion of thyroid hormones. It is commoner in females and may be associated with other autoimmune disorders.

1. **Presentation** is in the third to fourth decades with weight loss despite good appetite, increased bowel frequency, sweating, heat intolerance, nervousness, irritability, palpitations, weakness and fatigue.
2. **Signs**
   a. External
   - Diffuse thyroid enlargement (Fig. 20.99), fine hand tremor, palmar erythema, and warm and sweaty skin.
   - Finger clubbing (thyroid acropachy) (Fig. 20.100) and onycholysis (Plummer nails).
   - Alopecia, vitiligo (Fig. 20.101) and pretibial myxoedema (Fig. 20.102).
   - Myopathic proximal muscle weakness but brisk tendon reflexes.

   b. Cardiovascular
   - Sinus tachycardia, atrial fibrillation and premature ventricular beats.
   - High-output heart failure.
3. **Diagnostic tests.** Abnormal thyroid function: serum T_3, T_4, TSH, thyroxine-binding globulin (TBG) and thyroid-stimulating immunoglobulin (TSI).
4. **Treatment** options include carbimazole, propylthiouracil, propranolol, radioactive iodine and partial thyroidectomy.

Fig. 20.100
Thyroid acropachy

Fig. 20.101
Vitiligo

5. **Ophthalmic features**
   a. Common. Lid retraction, chemosis and proptosis.
   b. Uncommon. Superior limbic keratoconjunctivitis keratoconjunctivitis sicca and diplopia.
   c. Rare. Optic neuropathy and choroidal folds.

Fig. 20.102
Pretibial myxoedema

Fig. 20.103
Tuberculosis involving the cervical lymph glands

Fig. 20.104
Tuberculous involvement of the right hip

Tuberculosis

Tuberculosis (TB) is a chronic granulomatous infection caused by the tubercule bacillus, either bovine (*Mycobacterium bovis*) or human (*Mycobacterium tuberculosis*). The former is acquired by drinking milk from infected cattle and the latter by 'droplet infection'. Immunocompromised patients carry an increased risk of TB.

1. **Primary TB** occurs in subjects not previously exposed to the bacillus. It is characterized by the 'primary complex' in the chest (Ghon focus + regional lymphadenopathy), which causes few if any symptoms and usually heals spontaneously.
2. **Post-primary TB** is the result of reinfection or recrudescence of a primary lesion, usually in a patient with impaired immunity. Clinical features include erythema nodosum, fibrocaseous pulmonary lesions and lymph node involvement (Fig. 20.103). Haematogenous spread (miliary TB) may involve many internal organs and bones (Fig. 20.104).
3. **Diagnostic tests**
   a. ***Sputum examination*** for acid-fast bacilli.
   b. ***Chest radiographs.***
   c. ***Tuberculin*** testing may be useful in the diagnosis of extrathoracic TB. A negative result usually excludes TB, whereas a positive result does not necessarily distinguish between previous exposure and active disease. This is because most individuals have already received Bacille Calmette-Guerin (BCG) and will therefore exhibit a hypersensitivity response.
   d. ***Anticord factor antibody*** is a new test for ocular TB.
4. **Treatment** is initially with at least three drugs (isoniazid, rifampicin, pyrazinamide or ethambutol) and then with isoniazid and rifampicin.
5. **Ophthalmic features**
   a. *Uncommon*. Granulomatous anterior uveitis, multifocal choroiditis and retinal periphlebitis.
   b. *Rare*. Solitary choroidal granulomas.

Tuberous sclerosis

Tuberous sclerosis (Bourneville disease) is a phacomatosis characterized by the triad of (a) *epilepsy*, (b) *mental retardation* and (c) *adenoma sebaceum*, although not all features are invariably present.

1. **Inheritance** is AD.
2. **Signs**
   a. *Skin*
   - Adenoma sebaceum, consisting of fibroangiomatous red papules with a butterfly distribution around the nose and cheeks, is universal (Fig. 20.105).
   - Ash leaf spots are hypopigmented patches on the trunk (Fig. 22.106), limbs and scalp. In infants with sparse skin pigmentation they are best detected using ultraviolet light, under which they fluoresce (Wood's lamp).

Fig. 20.105
Adenoma sebaceum in tuberous sclerosis

Fig. 20.106
Ash leaf spot in tuberous sclerosis

Fig. 20.107
Shagreen patches in tuberous sclerosis

Fig. 20.108
Extensive adenoma sebaceum and a fibrous plaque on the forehead in tuberous sclerosis

- Shagreen patches consist of diffuse thickening over the lumbar region (Fig. 20.107).
- Fibrous plaques on the forehead (Fig. 20.108).
- Skin tags (molluscum fibrosum pendulum).
- Café-au-lait spots.
- Subungual hamartomas (Fig. 20.109).

b. Neurological. Scattered astrocytic cerebral hamartomas are universal (Fig. 20.110).

c. Visceral hamartomas. Renal (angiomyolipomas) and cardiac (rhabdomyomas).

3. **Treatment** involves control of epilepsy and management of mental and behavioural disorder.
4. **Ophthalmic features**

a. Common. Retinal astrocytomas in 50%.

b. Uncommon. Hypopigmented spots on the iris and retina, papilloedema and sixth nerve palsy may develop due to raised intracranial pressure.

Fig. 20.109
Subungual hamartoma on the little toe in tuberous sclerosis

Fig. 20.110
Axial CT scan showing a periventricular astrocytic hamartoma (Courtesy of K. Nischal)

Fig. 20.111
Ulcerative colitis

Ulcerative colitis

Ulcerative colitis is an idiopathic, chronic, relapsing inflammatory disease, involving the rectum and extending proximally to involve part or all of the large intestine. The disease is characterized by diffuse surface ulceration of the mucosa with the development of crypt abscesses and pseudopolyps (Fig. 20.111). Patients with long-standing disease carry an increased risk of developing carcinoma of the colon.

1. **Presentation** is in the second to third decades with bloody diarrhoea, lower abdominal cramps, urgency and tenesmus. Constitutional symptoms include tiredness, weight loss, malaise and fever.
2. **Extra-intestinal signs**
   a. ***Mucocutaneous***. Oral aphthous ulceration, erythema nodosum and pyoderma gangrenosum.
   b. ***Skeletal***. Finger clubbing, asymmetrical lower limb arthritis, sacroiliitis and ankylosing spondylitis.
   c. ***Hepatic***. Autoimmune hepatitis, sclerosing cholangitis and cholangiocarcinoma.
   d. ***Vascular***. Arterial and venous thrombosis.
3. **Diagnostic tests**. Endoscopy and biopsy.
4. **Treatment** options include systemic steroids, sulphasalazine, immunosuppressive agents and colectomy.
5. **Ophthalmic features**
   a. ***Uncommon***. Acute anterior uveitis, peripheral corneal infiltrates and conjunctivitis.
   b. ***Rare***. Papillitis.

Vogt–Koyanagi–Harada syndrome

Vogt–Koyanagi–Harada (V-K-H) syndrome is an idiopathic, multisystem disorder which typically affects Hispanics, Japanese and pigmented individuals. Japanese patients have an increased prevalence of HLA-DR4 and Dw15. In practice, V-K-H can be subdivided into Vogt–Koyanagi disease, characterized mainly by skin changes and anterior uveitis, and Harada disease, in which neurological features and exudative retinal detachments predominate.

1. **Prodromal phase** lasting a few days is characterized by neurological and auditory manifestations.
   a. ***Meningitis*** causing headache and neck stiffness.
   b. ***Encephalopathy*** is less frequent and may manifest as convulsions, paresis and cranial nerve palsies.
   c. ***Auditory features*** include tinnitus, vertigo and deafness.
2. **Acute uveitic phase** follows soon thereafter and is characterized by bilateral granulomatous anterior or multifocal posterior uveitis and exudative retinal detachments.
3. **Convalescent phase** follows several weeks later and is characterized by:
   - Localized alopecia, poliosis and vitiligo (Fig. 20.112).
   - Focal depigmented fundus lesions (sunset glow fundus) and depigmented limbal lesions (Sugiura sign).
4. **Chronic–recurrent phase** is characterized by smouldering anterior uveitis with exacerbations.
5. **Diagnostic criteria** must include at least three of the following:
   - Bilateral chronic anterior uveitis.
   - Posterior uveitis, including exudative retinal detachment, disc swelling and 'sunset glow fundus'.
   - Neurological features.
   - Cutaneous lesions.
6. **Treatment** is with systemic steroids.

von Hippel–Lindau syndrome

von Hippel–Lindau syndrome is a life-threatening phacomatosis.

Fig. 20.112
Vitiligo in Vogt–Koyanagi–Harada syndrome

1. **Inheritance** is AD.
2. **Signs**
   a. Tumours
   - Haemangioblastomas of the cerebellum, spinal cord (Fig. 20.113), medulla or pons.
   - Renal carcinoma (Fig. 20.114) and phaeochromocytoma.

   b. Cysts. Renal, pancreatic, hepatic, epididymal, ovarian and pulmonary.
   c. Polycythaemia.
3. **Ophthalmic features**. Capillary haemangiomas of the retina or optic nerve head.

Fig. 20.114
Axial CT scan of the abdomen showing a large renal carcinoma in von Hippel–Lindau syndrome (Courtesy of G. Wilkinson)

Fig. 20.113
MRI scan showing a haemangioblastoma of the upper cervical cord in von Hippel–Lindau syndrome (Courtesy of D. Thomas)

Wegener granulomatosis

Wegener granulomatosis is an idiopathic, multisystem, granulomatous disorder characterized by generalized small-vessel vasculitis affecting predominantly the respiratory tract and the kidneys. It affects males more commonly than females.

1. **Presentation** is in the fifth decade, often with pulmonary symptoms.

Fig. 20.115
Chest radiograph showing cavitation in Wegener granulomatosis (Courtesy of S. Ghiacy)

2. Signs

a. Respiratory tract

- Upper respiratory tract involvement by necrotizing granulomatous inflammation may result in perforation of the nasal septum, saddle-shaped nasal deformity and nasal–paranasal fistulae.
- Lower respiratory tract involvement may result in nodular lesions, infiltrates and cavitation with fluid levels (Fig. 20.115).

b. Organs

- Necrotizing glomerulonephritis, with renal failure.
- Focal vasculitis involving the spleen, heart and adrenals.

c. Neurological. Polyneuritis and meningoencephalitis.

3. Diagnostic tests. Anti-neutrophil cytoplasm antibodies (c-ANCA) are found in over 90% of patients with active disease.

4. Treatment is with systemic steroids and cyclophosphamide.

5. Ophthalmic features

a. Common. Nasolacrimal obstruction and dacryocystitis.

b. Uncommon. Scleritis and peripheral ulcerative keratitis.

c. Rare. Orbital pseudo-tumour and occlusive retinal periarteritis.

CHAPTER 20

Systemic Diseases

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Acromegaly

Acromegaly is caused by excessive growth hormone (GH) occurring during adult life, after epiphyseal closure, and is almost invariably due to a secreting pituitary acidophil adenoma. (Hypersecretion of growth hormone in childhood, prior to epiphyseal closure, results in gigantism.)

1. **Presentation** is in the fourth to fifth decades.
2. **Signs**
   - *a. Skin.* Hyperhidrosis, seborrhoea, acne and in females hirsutism.
   - *b. Face.* Coarseness of features: thick lips, exaggerated nasolabial folds, prominent supraorbital ridges (Fig. 20.1) and enlargement of the lower jaw (prognathism) (Fig. 20.2) with dental malocclusion.
   - *c. Enlargement* of the head, hands, feet, tongue (Fig. 20.3) and internal organs.
3. **Complications** include osteoarthritis (Fig. 20.4), carpal tunnel syndrome, cardiomyopathy, hypertension, respiratory disease, diabetes mellitus, gonadal dysfunction and neuropathy.
4. **Diagnostic tests.** The diagnosis may be confirmed by noting GH levels in response to an oral glucose tolerance test. Normal individuals manifest suppression of GH levels to below 2 mU/l. However, in acromegaly, GH levels do not fall, and may paradoxically rise.
5. **Treatment** options include bromocriptine (a long-acting dopamine agonist), radiotherapy (external beam or by implantation of yttrium rods in the pituitary) and transsphenoidal hypophysectomy.

Fig. 20.1
Acromegaly

Fig. 20.2
Plain skull radiograph of acromegaly showing an enlarged mandible with widening of the mandibular angle (prognathism), enlarged frontal sinus, thickening of the skull vault and an expanded pituitary fossa (Courtesy of S. Ghiacy)

Fig. 20.3
Macroglossia in acromegaly

Fig. 20.4
Plain radiograph of the hands in acromegaly showing lips and hooks of the terminal phalanges, enlarged bones with prominent muscle attachments and early osteoarthritic changes (Courtesy of S. Ghiacy)

6. Ophthalmic features

a. Common. Bitemporal hemianopia and optic atrophy.

b. Rare. Angioid streaks and see-saw nystagmus of Maddox.

Acquired immunodeficiency syndrome

Acquired immunodeficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV), which is predominantly transmitted by sexual intercourse and occasionally by contaminated blood or needles. On a worldwide basis, heterosexual intercourse is the predominant mode of transmission; in the Western world, however, AIDS is commonly transmitted by homosexual contact. Transmission may also occur transplacentally or via breast milk. Infection with HIV is typically followed by a latent period, after which develop the clinical manifestations of AIDS. HIV targets CD4+T-(helper) lymphocytes, which are vital to the initiation of the immune response to pathogens. A steady decline in the absolute number of CD4+T-lymphocytes therefore occurs, resulting in progressive immune deficiency, particularly that of cell-mediated immunity. Regular estimation of the CD4+T count is therefore a useful measure of disease progression. Apart from immunodeficiency, HIV also has the property of mediating direct damage to the central nervous system.

1. Presentation

a. Acute seroconversion illness. HIV infection is sometimes followed a few weeks later by constitutional symptoms such as fever, headache, malaise and a maculopapular rash, associated with generalized lymphadenopathy, soon after which anti-HIV antibodies appear.

b. An asymptomatic phase, often lasting many years, then follows, during which steady depletion of CD4+T-lymphocytes occurs.

c. Symptomatic HIV infection (AIDS) then follows, characterized by immunosuppression with opportunistic infections and tissue damage directly due to HIV infection.

2. Opportunistic infections in AIDS include:

a. Protozoan. Toxoplasma, cryptosporidium, microsporidium and *Pneumocystis carinii*.

b. Viral. Cytomegalovirus, herpes simplex and zoster, molluscum contagiosum and Epstein–Barr.

c. Fungal. Cryptococcus, candida (Fig. 20.5) and histoplasma.

d. Bacterial. *Mycobacterium tuberculosis*, *Mycobacterium avium*, staphylococci, streptococci, *Haemophilus* and *Bartonella henselae*.

3. Tumours include Kaposi sarcoma (Fig. 20.6), non-Hodgkin B-cell lymphoma and squamous cell carcinoma of the cervix and anus.

4. Other manifestations include HIV wasting syndrome, encephalopathy and progressive multifocal leucoencephalopathy.

5. Diagnostic tests. Serological testing for HIV infection should be performed only with informed consent after proper counselling, due to the profound implications of a positive result. HIV is confirmed most commonly by the demonstration of anti-HIV antibodies in the serum, by the ELISA and western blot tests. 'Seroconversion' may take 3 months or longer to occur following exposure to the virus, sometimes necessitating serial testing in individuals at high risk. Subsequent to the establishment of HIV positivity, CD4+T-lymphocyte counts are measured every 3 months. A CD4+T-lymphocyte count $< 200/mm^3$ implies a high risk of HIV-related disease. AIDS is diagnosed when an HIV-positive subject develops one or more of a defined list of indicator diseases (Table 20.1).

Fig. 20.5
Oral candidiasis in AIDS

Fig. 20.6
Kaposi sarcoma in AIDS

6. Treatment. Although there is no cure for AIDS, the progression of disease can be slowed by a number of drugs. The aim of treatment is to reduce the plasma viral load. Ideally therapy should be commenced before the development of irreversible damage to the immune system.

a. Indications for commencement of anti-HIV therapy include:

- Symptomatic HIV disease.
- CD4+T-lymphocyte count $< 300/mm^3$.
- Rapidly falling CD4+T-lymphocyte count.
- Viral load $> 10,000$/ml of plasma.

b. Drug treatment is with 'highly active antiretroviral therapy' (HAART), which involves two nucleoside reverse

Table 20.1 AIDS-defining diagnoses (1993 Classification, Europe)

- Candidiasis of bronchi, trachea, lungs or oesophagus
- Cervical carcinoma, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcus, extrapulmonary
- Cryptosporidiosis, with diarrhoea for >1 month
- Cytomegalovirus disease other than in liver, spleen or lymph nodes
- Encephalopathy, HIV-related
- Herpes simplex ulcers for 1 month or bronchitis, pneumonitis or oesophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, with diarrhoea for >1 month
- Kaposi sarcoma
- Lymphoid interstitial pneumonitis
- *Mycobacterium avium* complex or *M. kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Pneumonia, recurrent
- Progressive multifocal leucoencephalopathy
- Salmonella (non-typhoid) septicaemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV (weight loss >10% baseline with no other identified cause)

transcriptase inhibitors with either a non-nucleoside reverse transcriptase inhibitor or one or two protease inhibitors.

- Nucleoside reverse transcriptase inhibitors include zidovudine, lamivudine and zalcitabine.
- Protease inhibitors include amprenavir, indinavir and nelfinadir.
- Non-nucleoside reverse transcriptase inhibitors include efavirenz and nevirapine.

NB: Antiretroviral therapy is continuously evolving and should therefore be left to a trained physician.

7. Ophthalmic features

*a. **Eyelids.*** Kaposi sarcoma, multiple molluscum lesions and severe herpes zoster ophthalmicus.

*b. **Orbit.*** Cellulitis usually from contiguous sinus infection and B-cell lymphoma.

*c. **Conjunctiva.*** Kaposi sarcoma, squamous cell carcinoma and microangiopathy.

*d. **Cornea.*** Keratitis due to microsporidium, herpes simplex and herpes zoster.

*e. **Keratoconjunctivitis sicca.***

*f. **Anterior uveitis.***

*g. **HIV retinopathy*** (cotton wool spots).

*h. **Retinitis.*** Cytomegalovirus, varicella zoster (progressive outer retinal necrosis) and toxoplasma.

*i. **Choroiditis.*** Pneumocystis and cryptococcus.

*j. **B-cell intraocular lymphoma.***

Ankylosing spondylitis

Ankylosing spondylitis (AS) is a spondarthropathy, primarily involving inflammation, calcification and finally ossification of ligaments and capsules of joints, with resultant bony ankylosis of the axial skeleton. It typically affects males, 90% of whom are HLA-B27 positive.

1. Presentation is in early adulthood with insidious onset of pain and stiffness in the lower back or buttocks. This is initially worse after inactivity, but may be aggravated by weight bearing.

2. Signs

*a. **Arthritis.*** In order of frequency, the joints most affected are the sacro-iliac, spine, hips, ribs and shoulders.

Fig. 20.7
Limitation of spinal flexion in advanced ankylosing spondylitis

Fig. 20.8
Severe spinal involvement in ankylosing spondylitis with bony bridging by syndesmophytes ('bamboo spine') (Courtesy of S. Ghaey)

Progressive limitation of spinal movements occurs (Fig. 20.7); the spine characteristically becomes fixed in flexion. Reduced mobility of the thoracic cage may predispose to pulmonary infection.

b. Enthesopathy of the plantar fascia and Achilles tendon.

3. **Associations.** Inflammatory bowel disease (colitic arthritis).
4. **Complications.** Apical pulmonary fibrosis, aortic incompetence and cardiac conduction defects.
5. **Diagnostic tests.** The ESR is raised. Radiology of the sacro-iliac joints reveals juxta-articular osteoporosis in the early stages, later followed by sclerosis and bony obliteration of the joint. The spinal ligaments may also manifest calcification ('bamboo spine') (Fig. 20.8), as may other joints involved by the inflammatory process.
   NB: Radiological changes often pre-date clinical symptoms.
6. **Treatment** options include physiotherapy, NSAIDs, sulphasalazine and intra-articular steroid injections. Surgical correction of bony deformities may be necessary.
7. **Ophthalmic features.** Acute anterior uveitis in 30%.

Atopic eczema

Atopic eczema (dermatitis) is an idiopathic, often familial, skin condition, which may be associated with asthma and hay fever.

1. **Presentation** is with intense pruritus usually in infancy, but may be at any age.
2. **Signs**
   a. Facial eczema is usually seen in infants and consists of itchy, dry, erythematous papules (Fig. 20.9).
   b. Flexural eczema (Fig. 20.10) usually develops later with symmetrical involvement of the elbow and knee flexures, wrists and ankles by dry, lichenified or excoriated skin.
3. **Treatment** options include emollients, coal-tar preparations and topical steroids.
4. **Ophthalmic features**
   a. Common. Madarosis and staphylococcal blepharitis.

Fig. 20.9
Infantile eczema

Fig. 20.10
Adult eczema

b. Uncommon. Chronic keratoconjunctivitis, keratoconus and early-onset cataract.
c. Rare. Retinal detachment.

Behçet disease

Behçet disease is an idiopathic, recurrent, multisystem disease. It typically affects young men from the eastern Mediterranean region and Japan and is associated with HLA-B51 and its subtype HLA-Bw51.

1. **Presentation** is in the third to fourth decades with localized lesions such as aphthous ulceration.
2. **Major diagnostic criteria**
   a. Recurrent oral aphthous stomatitis is universal. A typical aphthous ulcer is painful and shallow with a yellowish necrotic base. They occur in crops on the tongue (Fig. 20.11), gums, lips and buccal mucosa.
   b. Skin lesions include erythema nodosum (Fig. 20.12), acneiform (Fig. 20.13), subcutaneous thrombophlebitis, a papulo-vesiculo-pustular rash and hypersensitivity.

Fig. 20.11
Aphthous ulceration in Behçet disease

The latter can be tested with a 'prick' (pathergy) test, in which a pustule appears after puncturing the skin with a needle (Fig. 20.14) or by stroking the skin and demonstrating the appearance of corresponding lines (dermatographism) (Fig. 20.15).

Fig. 20.12
Erythema nodosum-like skin lesions in Behçet disease (Courtesy of B. Noble)

Fig. 20.13
Acneiform skin lesions in Behçet disease (Courtesy of B. Noble)

Fig. 20.14
Pustule formed following pricking in Behçet disease (positive pathergy test) (Courtesy of B. Noble)

Fig. 20.15
Cutaneous hypersensitivity demonstrated by stroking the skin (dermatographism) in Behçet disease (Courtesy of B. Noble)

Fig. 20.16
Genital ulceration in Behçet disease

c. ***Recurrent genital ulceration*** of the penis (Fig. 20.16) and scrotum in males and of the labia and vagina in females.
d. ***Uveitis***, both anterior and posterior.

Fig. 20.17
Dilated superficial veins secondary to deep obliterative thrombophlebitis in Behçet disease. (Courtesy of B. Noble)

3. **Minor diagnostic criteria**
   a. *Arthritis* involving the knees, ankles and occasionally the sacro-iliac joints.
   b. *Epididymitis*.
   c. *Intestinal ulceration*.
   d. *Vascular*. Obliterative thrombophlebitis of superficial and deep veins (Fig. 20.17), large vessel arterial occlusion and aneurysm formation.
   e. *Neurological*. Brain stem syndromes and meningoencephalitis.
4. **Complete Behçet disease**. Four major criteria occurring simultaneously or at different times.
5. **Incomplete Behçet disease**. One of the following:
   - Three major criteria.
   - Two major plus two minor criteria.
   - Uveitis plus another major criterion.
   - Uveitis plus two minor criteria.
6. **Treatment**
   a. *Topical* tetracycline or steroids for local lesions such as oral or genital ulcers.
   b. *Systemic* therapeutic options include steroids, often in combination with colchicine, azathioprine, cyclosporin, chlorambucil and levamisole.
7. **Ophthalmic features**
   a. *Common*. Anterior uveitis, vitritis and retinitis.
   b. *Uncommon*. Occlusive retinal periphlebitis, periarteritis and retinal oedema.

Carotid stenosis

Carotid stenosis involves atheromatous narrowing, often associated with ulceration, at the bifurcation of the common carotid artery. The irregularity of the vessel wall may act as a source of cerebral and retinal emboli composed of platelets and fibrin (white emboli) or tiny fragments of atheromatous material (Hollenhorst plaques).

1. **Presentation** is in the seventh to ninth decades with:
   - Transient retinal ischaemic attacks (amaurosis fugax).
   - Retinal artery occlusion.
   - Transient cerebral ischaemic attacks (TIA).
   - Stroke.
   - Ocular ischaemic syndrome.
   - Asymmetrical diabetic retinopathy—the ipsilateral eye tends to be relatively spared.
2. **Signs**
   a. *Palpation* of the cervical carotid arteries should be done gently to avoid dislodging a thrombus. Severe or complete stenosis is associated with a diminished or absent carotid pulse. Other peripheral pulses may also be diminished in generalized atherosclerosis.
   b. *Auscultation* over a partial stenosis gives rise to a bruit, best detected with the bell of the stethoscope. It is important to auscultate along the entire length of the artery and to ask the patient to hold his breath. The most ominous bruit is one that is high-pitched and soft because it indicates tight stenosis. When the lumen is narrowed by 90% or more, the bruit disappears.
3. **Diagnostic tests**
   a. *Duplex scanning* is a non-invasive screening test involving a combination of high-resolution real-time ultrasonography with Doppler flow analysis (Fig. 20.18).
   b. *Magnetic resonance angiography* is non-invasive and accurate (Fig. 20.19).
   c. *Carotid arteriography* is the most accurate method (Fig. 20.20) but carries a significant risk of complications. Resolution can be further improved by digitally removing (subtracting) the distracting background, leaving only the arterial image (Fig. 20.21).
4. **Treatment** is aimed at preventing stroke and permanent visual impairment by the following:
   a. *General measures* addressing associated risk factors such as smoking, hypertension, diabetes, obesity, hypercholesterolaemia and cardiac arrhythmias.

Fig. 20.18
Colour Doppler ultrasonogram showing carotid stenosis

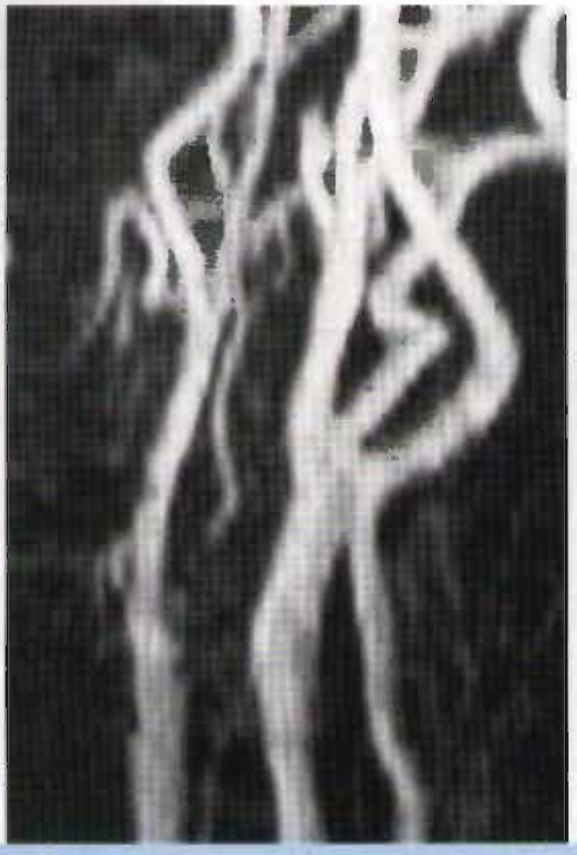

Fig. 20.19
MRA showing severe stenosis of the right internal carotid artery (Courtesy of D. Thomas)

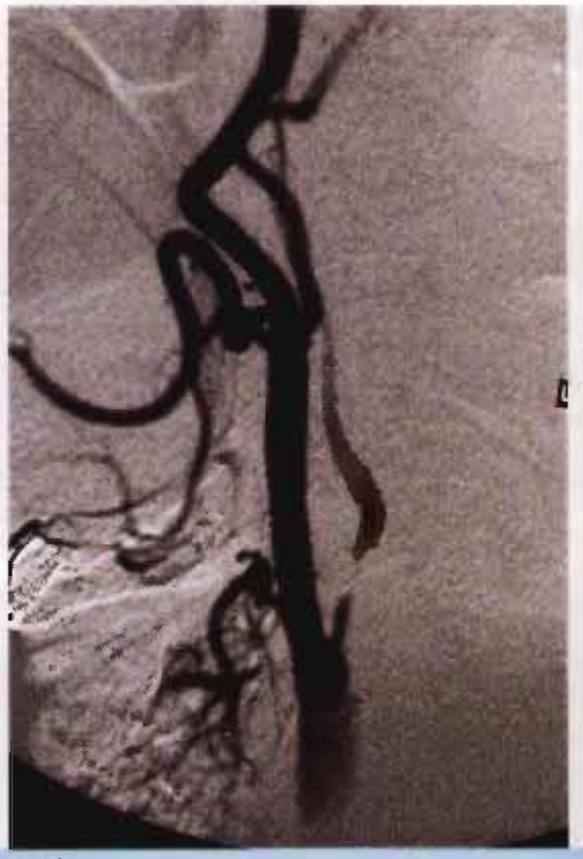

Fig. 20.21
Digital subtraction arteriogram showing severe stenosis of the right internal carotid artery (Courtesy of D. Thomas)

Fig. 20.20
Arteriogram without subtraction showing severe stenosis of the right internal carotid artery (Courtesy of D. Thomas)

b. Antiplatelet therapy.
- Aspirin 75–300 mg daily.
- Combined aspirin and dipyridamole (Persantin) 200 mg daily, if aspirin alone is ineffective.
- Clopidogrel (Plavix) 75 mg daily if other measures fail.

c. Oral anticoagulants such as warfarin, if TIAs continue despite antiplatelet therapy.

d. Carotid endarterectomy (Fig. 20.22) is indicated in patients with symptomatic stenosis greater than 70%.

5. Ophthalmic features

a. Common. Amaurosis fugax.

b. Uncommon. Hollenhorst plaques and retinal artery occlusion.

c. Rare. Hypotensive (slow flow) retinopathy and ocular ischaemic syndrome

Cat-scratch disease

Cat-scratch disease (fever) is a subacute infection caused by a small Gram-negative bacillus, *Bartonella henselae*, transmitted by a scratch or bite of an infected animal, often a cat.

1. Presentation is at any age with a pustule at the site of inoculation followed by constitutional symptoms, lymphadenopathy and erythema nodosum.

Fig. 20.22
Scar following carotid endarterectomy

2. **Disseminated disease** is rare but may affect immunocompromised individuals. It is characterized by encephalitis, hepatitis, pneumonia, splenomegaly, splenic abscess formation and osteomyelitis.
3. **Diagnostic tests** include blood cultures and immunofluorescent antibody titres.
4. **Treatment** is with oral doxycycline and rifampicin; the organism is also sensitive to ciprofloxacin and co-trimoxazole.
5. **Ophthalmic features**
   a. Uncommon. Neuroretinitis.
   b. Rare. Parinaud oculoglandular syndrome, intermediate uveitis, acute multifocal retinitis, retinal periphlebitis and exudative retinal detachment.

Chlamydial genital infection

Chlamydial genital infection is sexually transmitted and caused by serotypes D–K of *Chlamydia trachomatis*.

1. **In males** chlamydial infection is the most common cause of 'non-specific urethritis' (NSU) and 'non-gonococcal urethritis' (NGU). It may also cause epididymitis and act as a trigger for Reiter disease.
2. **In females** chlamydia may cause abacterial pyuria, cervicitis, salpingitis, peritonitis and perihepatitis (Fitz-Hugh–Curtis syndrome). Chronic salpingitis may result in infertility.
3. **Treatment**. Doxycycline 100 mg b.d. for 7 days or a single dose of azithromycin 1000 mg.
4. **Ophthalmic features**
   a. Uncommon. Adult conjunctivitis.
   b. Rare. Neonatal conjunctivitis.

Cicatricial pemphigoid

Cicatricial pemphigoid (benign mucous membrane pemphigoid) is a chronic autoimmune (type 2 hypersensitivity) disease characterized by recurrent blisters of the mucous membranes and skin. It affects women twice as often as men and is associated with an increased prevalence of HLA-B12.

Fig. 20.23
Oral involvement in cicatricial pemphigoid

1. **Presentation** is in the seventh to eighth decades with ocular or mucocutaneous lesions or both.
2. **Signs**
   a. Mucosal blisters, most frequently oral (Fig. 20.23), rupture within a day or two, leaving erosions and ulcers which heal without scarring. Other sites include the nose, larynx, oesophagus, anus, vagina, glans penis and urethra; ulcers at these sites heal with scarring and may result in stricture formation.
   b. Skin lesions are less common and are of two types.
   - Recurrent, non-scarring blisters which may involve the groins and/or extremities (Fig. 20.24) and may occasionally become generalized.
   - Sparse, localized erythematous plaques associated with recurrent scarring blisters on the scalp and skin near affected mucous membranes.
3. **Treatment**
   a. Local oral lesions may be treated with topical steroids.
   b. Widespread involvement, particularly of the eyes, requires systemic steroids, azathioprine, dapsone or intravenous immunoglobulin.
4. **Ophthalmic features**. Cicatrizing conjunctivitis in the vast majority of cases.

Fig. 20.24
Cutaneous involvement in cicatricial pemphigoid

Fig. 20.26
Glossitis in Crohn disease

Crohn disease

Crohn disease (regional ileitis) is an idiopathic, chronic, relapsing disease characterized by multifocal, full-thickness, non-caseating granulomatous inflammation of the intestinal wall. It most frequently involves the ileocaecal region (Fig. 20.25) but any area of the bowel, including the mouth, may be affected.

1. **Presentation** is in the second to third decades with fever, weight loss, diarrhoea and abdominal pain.
2. **Extra-intestinal manifestations**
   a. Oral. Glossitis (Fig. 20.26) and aphthous ulceration.
   b. Cutaneous. Erythema nodosum, pyoderma gangrenosum (Fig. 20.27) and psoriasis.
   c. Skeletal. Finger clubbing, acute peripheral arthritis, sacroiliitis and ankylosing spondylitis.
3. **Complications** include intestinal obstruction due to stricture formation (Fig. 20.28), perirectal fistulae, abscesses and fissures, and liver disease.
4. **Diagnostic tests** include endoscopy and biopsy.

Fig. 20.27
Pyoderma gangrenosum in Crohn disease

5. **Treatment** options include nutritional support, steroids, antibiotics, immunosuppressives and surgery.
6. **Ophthalmic features**
   a. Uncommon. Acute anterior uveitis, conjunctivitis, episcleritis and peripheral corneal infiltrates.
   b. Rare. Retinal periphlebitis.

Fig. 20.25
Crohn disease involving the ileocaecal region

Cushing syndrome

Cushing syndrome is due to prolonged elevation of free plasma glucocorticoid levels.

1. **Causes**
   - Iatrogenic due to systemic administration of steroids (most common).
   - Hypersecretion of glucocorticoids by the adrenal cortex.
   - Hypersecretion of ACTH by a pituitary basophil adenoma (Cushing disease).
2. **Signs**
   a. Obesity may be generalized or classically involve the trunk, abdomen and neck (buffalo hump).

Fig. 20.28
Barium enema showing stricture and 'rose thorn' ulceration in Crohn disease (Courtesy of S. Ghiacy)

Fig. 20.29
Moon face, hyperpigmentation and hirsutism in Cushing syndrome

b. The face is swollen (moon face) and the complexion plethoric. Females may be hirsute (Fig. 20.29).

c. The skin is thin and susceptible to bruising. Purple striae may be seen (Fig. 20.30). Hyperpigmentation may develop with (ACTH-dependent) Cushing disease.

d. Other features include depression/psychosis, osteoporosis, poor wound healing and proximal myopathy.

3. **Complications** include hypertension, diabetes, pathological fractures and acute necrosis of the femoral head.
4. **Diagnostic tests** are targeted at first establishing the presence of elevated cortisol levels and then identifying the underlying cause (unless iatrogenic); they are best undertaken by an endocrinologist.

Fig. 20.30
Obesity and cutaneous striae in Cushing syndrome

5. **Treatment**
   a. Surgical removal of pituitary adenoma or adrenal secreting tumour. Ectopic foci of ACTH secretion may also be amenable to excision.
   b. Medical suppression of cortisol secretion with metyrapone or aminoglutethimide.
6. **Ophthalmic features**
   a. Common. Steroid-induced cataracts frequently develop in iatrogenic Cushing syndrome but not in Cushing disease.
   b. Uncommon. Bitemporal hemianopia is uncommon with secreting pituitary tumours, which tend to present with systemic features of hypersecretion, as opposed to non-secreting pituitary tumours, which tend to present with chiasmal compression. Glaucoma may develop in susceptible individuals with iatrogenic Cushing syndrome.

Diabetes mellitus

Diabetes mellitus is a common metabolic disorder characterized by sustained hyperglycaemia of varying severity secondary to lack, diminished efficacy, or both of endogenous insulin. The disease affects about 2% of the population in the UK. Despite some degree of overlap, diabetes can be divided into two types:

1. **Type 1** diabetes (insulin-dependent diabetes mellitus, IDDM, juvenile-onset diabetes) develops most frequently between the ages of 10 and 20 years, with acute symptoms of polydipsia, polyuria, nocturia and weight loss. There is an association with HLA-DR3 and -DR4. Autoimmune destruction of pancreatic islet cells is postulated as instrumental in pathogenesis. Type 1 diabetics are often lean and manifest a total lack of insulin; they may develop keto-acidosis and require insulin for glycaemic control.
2. **Type 2** diabetes (non-insulin-dependent diabetes mellitus, NIDDM, maturity-onset diabetes), on the other hand,

develops most frequently between the ages of 50 and 70 years. Type 2 diabetics are often overweight and manifest relative deficiency of insulin and/or peripheral insulin resistance. Metabolic control commonly involves diet and oral anti-diabetic drugs. Some patients may subsequently require insulin for glycaemic control, although many remain non-insulin-dependent. Type 2 diabetes is often initially asymptomatic, and discovered by chance. Alternatively, it may present with recurrent infections of the skin, vulva or glans penis or, rarely, with complications such as vitreous haemorrhage.

3. **Diagnostic tests**
   - A fasting glucose concentration of >6.7 mmol/l.
   - A random glucose concentration of >10.0 mmol/l.
   - A glucose tolerance test is performed only if the diagnosis is uncertain.
   - Glycosylated haemoglobin (HBA1c) reflects the average level of blood glucose over the preceding 6 weeks. Normally 4–8% of haemoglobin is glycosylated; values in excess of this reflect inadequacy of glycaemic control and is a better indicator of the efficacy or otherwise of treatment than a single random glucose level.
   - Urine testing for glycosuria is a crude and unsatisfactory means of monitoring diabetic control.

   NB: Glycosuria per se does not necessarily imply diabetes, as it may merely reflect a lowered renal threshold for glucose excretion.
4. **Treatment**. Type 1 diabetics require insulin; type 2 diabetics require a regimen involving weight reduction, physical exercise and diet control, often in combination with either or both oral hypoglycaemic agents and insulin. Oral anti-diabetic drugs include sulphonylureas (e.g. gliclazide, glipizide) and biguanides (e.g. metformin). It is also important to aggressively treat any associated problems, particularly hypertension and hyperlipidaemia.
5. **Systemic complications**
   a. ***Renal***. Nephropathy is initially characterized by microscopic proteinuria. Severe renal disease may eventually result in renal failure requiring dialysis or transplantation.
   b. ***Vascular***. Accelerated atherosclerosis of coronary and lower limb arteries. Severe involvement of legs may result in ischaemic ulceration and gangrene of the feet and toes (Fig. 20.31).
   c. ***Neurological***
      - Sensory polyneuropathy principally affects the feet in a 'glove and stocking' distribution and may give rise to painless neuropathic perforating ulcers at pressure points in the soles (Fig. 20.32) and degenerative arthropathy (Charcot joints) (Fig. 20.33).
      - Cranial nerve palsies—classically the pupil-sparing third nerve palsy—may occur due to small vessel involvement.
   d. ***Skin*** manifestations include increased susceptibility to bacterial and fungal infections (Fig. 20.34), blistering of the feet and toes, necrobiosis lipoidica (Fig. 20.35) and lipodystrophy at sites of insulin injection (Fig. 20.36) and granuloma annulare.

Fig. 20.31
Diabetic gangrene

Fig. 20.32
Diabetic neuropathic ulceration

Fig. 20.33
Charcot joints

NB: Neuropathy in combination with vascular insufficiency and increased susceptibility to infection commonly results in gangrene of the extremities (diabetic foot).

Fig. 20.34
Moniliasis

Fig. 20.35
Necrobiosis lipoidica

Fig. 20.36
Diabetic lipodystrophy

6. **Ophthalmic features**
   a. ***Common***. Retinopathy and iridopathy (increased iris transillumination).
   b. ***Uncommon***. Changes in refraction, accelerated senile cataract, rubeosis iridis, ocular motor nerve palsies and asteroid hyalosis.
   c. ***Rare***. Papillopathy, pupillary light-near dissociation, acute-onset cataract and rhino-orbital mucormycosis.

Ehlers–Danlos syndrome type 6 (ocular sclerotic)

Ehlers–Danlos syndrome is a connective tissue disorder involving genetically determined abnormalities of collagen. There are 11 subtypes but only type 6 is associated with ocular features.

1. **Inheritance** is AR.
2. **Signs**
   a. ***Skin***. Thinning, hyperelasticity (Fig. 20.37), bruising and slow healing.
   b. ***Joints***. Hyperextensibility, easy dislocation, repeated falls, hydroarthrosis and pseudo-tumour formation over the knees and elbows.
   c. ***Vascular***. Bleeding diathesis, dissecting aortic aneurysm, spontaneous rupture of large blood vessels and mitral valve prolapse.
3. **Ophthalmic features**
   a. ***Common***. Ocular fragility with increased vulnerability to minimal trauma, blue sclera and microcornea.
   b. ***Uncommon***. Ectopia lentis, keratoconus, cornea plana, high myopia, retinal detachment and angioid streaks.

Fig. 20.37
Cutaneous hyperelasticity in Ehlers–Danlos syndrome

Giant cell arteritis

Giant cell arteritis (GCA) is a granulomatous necrotizing arteritis (Fig. 20.38) with a predilection for large and medium-size arteries, particularly the superficial temporal, ophthalmic, posterior ciliary and proximal vertebral. The severity and extent of involvement are associated with the quantity of elastic tissue in the media and adventitia. Intracranial arteries, which possess little elastic tissue, are usually spared.

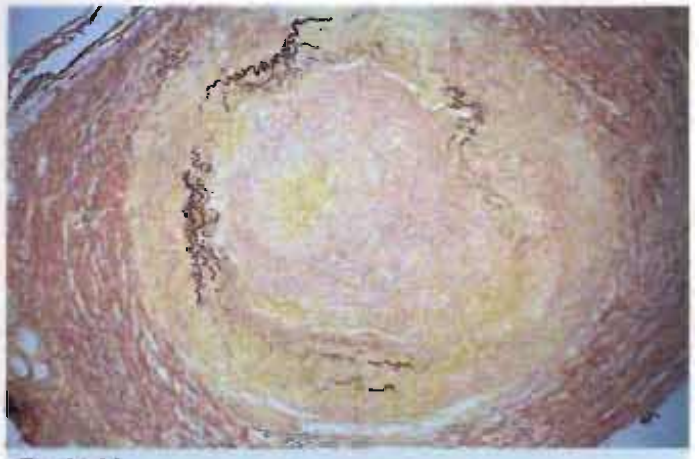

Fig. 20.38
Histology of giant cell arteritis showing granulomatous infiltration, disruption of the internal elastic lamina, proliferation of the intima and complete occlusion of the lumen (Courtesy of A. Garner)

Fig. 20.39
Dilated and tortuous superficial temporal artery in giant cell arteritis

Fig. 20.40
Scalp necrosis in giant cell arteritis

1. **Presentation** is usually in the seventh to eighth decades with the following:
   a. ***Scalp tenderness***, first noticed when combing the hair, is a frequent presenting complaint.
   b. ***Headache***, sometimes severe, may be localized to the frontal, occipital or temporal areas, or more generalized.
   c. ***Jaw claudication*** is virtually pathognomonic. It is caused by ischaemia of the masseter and causes pain on speaking and chewing.
   d. ***Polymyalgia rheumatica*** is characterized by pain and stiffness in proximal muscle groups (typically the shoulders). It is characteristically worse in the morning and after exertion and may precede cranial symptoms by many months.
   e. ***Non-specific symptoms*** such as neck pain, weight loss, fever, night sweats, malaise and depression are common.
   f. ***Blindness*** of sudden onset with minimal systemic upset (occult arteritis) is uncommon.
2. **Other features**
   a. ***Superficial temporal arteritis*** is characterized by thickened, tender, inflamed and nodular arteries (Fig. 20.39), which cannot be flattened against the skull. Pulsation is initially present, but later ceases, a sign strongly suggestive of GCA, since a non-pulsatile superficial temporal artery is highly unusual in a normal individual. In very severe cases, scalp gangrene may ensue (Fig. 20.40).

> ***NB:*** The best location to examine pulsation is directly in front of the pinna.

   b. ***Complications***. Dissecting aneurysms, aortic incompetence, myocardial infarction, renal failure and brain stem stroke.
3. **Diagnostic tests**
   a. ***Erythrocyte sedimentation rate*** (ESR) is often very high, with levels of >60 mm/h. In interpreting the ESR the following should be borne in mind:
      - The normal ESR equals roughly half the age in men; it is 5 mm higher in women.
      - ESR levels of 40 mm/h may be 'normal' in diabetics and in the elderly.
      - Approximately 20% of patients with GCA have a normal ESR.
   b. ***C-reactive protein*** is invariably raised and may be helpful when ESR is equivocal.
   c. ***Temporal artery biopsy*** (TAB) should be performed if GCA is suspected.
      - Steroids should never be withheld pending biopsy, which should ideally be performed within 3 days of commencing steroids.
      - Systemic steroids for more than 7 days may suppress histological evidence of active arteritis; however, this is not invariable and biopsy should still be performed even if steroid therapy has been commenced considerably earlier. This is for two reasons: firstly, if positive it justifies long-term administration of steroids in a population highly prone to their adverse effects. If negative, it provides some justification for tailing off and stopping steroid therapy.

- In patients with ocular involvement it is advisable to take the biopsy from the ipsilateral side. The ideal location is the temple because it avoids damage to a major branch of the auriculotemporal nerve.
- At least 2.5 cm of the artery should be taken and serial sections examined because of the phenomenon of 'skip lesions': segments of histologically normal arterial wall may alternate with segments of granulomatous inflammation.
- Lack of pulsation may render TAB difficult, especially in inexperienced hands; not uncommonly, a segment of nerve is excised and sent for histological examination.

4. **Treatment** involves the administration of systemic steroids (*see* Chapter 18).
5. **Ophthalmic features**
   a. Common. Anterior ischaemic optic neuropathy.
   b. Uncommon. Amaurosis fugax, cotton wool spots, central retinal artery occlusion, cilioretinal artery occlusion and ocular motor nerve palsies (commonly a pupil-sparing third nerve palsy).
   c. Rare. Ocular ischaemic syndrome.

Homocystinuria

Homocystinuria is caused by deficiency of cystathionine-β-synthetase leading to accumulation of homocystine and methionine. The condition is phenotypically similar to Marfan syndrome but carries a thrombotic tendency.

1. **Inheritance** is AR.
2. **Signs**
   - Blond hair with a malar flush (Fig. 20.41).
   - Marfanoid habitus but infrequent arachnodactyly.
   - Mental retardation and psychiatric disturbance.

Fig. 20.41
Blond hair and a malar flush in homocystinuria

3. **Complications**
   - Osteoporosis and spontaneous crush fractures.
   - Thromboses in any vessel and at any age, particularly postoperatively or postpartum.
4. **Treatment** involves oral pyridoxine to reduce homocystine and methionine levels.
5. **Ophthalmic features**
   a. Common. Ectopia lentis.
   b. Uncommon. Myopia and retinal detachment.

Hypertension

Hypertension is most commonly idiopathic (essential) and occasionally secondary to a renal or metabolic disorder.

1. **Presentation** is usually in the fifth to sixth decades.
2. **Signs**. Elevation of blood pressure >140/90 (although the degree of elevation required to diagnose hypertension varies with age).
3. **Complications**
   - Left ventricular hypertrophy and subsequent failure.
   - Increased risk of atherosclerosis resulting in coronary heart disease and stroke.
   - Renal disease.
4. **Treatment** options include lifestyle modification (exercise, weight reduction, diminished salt intake and alcohol consumption) and drug therapy (diuretics, beta-blockers, calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists and alpha-blockers).
5. **Ophthalmic features**
   a. Common. Retinal arteriolosclerosis and branch retinal vein occlusion.
   b. Uncommon. Retinopathy, retinal artery occlusion, retinal artery macroaneurysm, anterior ischaemic optic neuropathy, choroidal infarcts and ocular motor nerve palsies.
   c. Rare. Exudative retinal detachment (in eclampsia).

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is an inflammatory arthritis of at least 3 months duration developing in children before the age of 16 years. The female:male ratio is 3:2. Patients are seronegative for IgM rheumatoid factor. In North America, however, JIA is frequently referred to as juvenile 'rheumatoid' arthritis.

1. **Presentation**. Based on the onset and the extent of joint involvement during the first 6 months, three types of presentation are recognized:
   a. Pauciarticular-onset JIA accounts for about 60% of cases. It affects girls five times as often as boys, with a peak age of onset of around 2 years. The arthritis involves four or fewer joints, most commonly the knees (Fig. 20.42), although the ankles and wrists may also be affected. Some patients in this subgroup remain pauciarticular, while others subsequently develop a

Fig. 20.42
Pauciarticular juvenile idiopathic arthritis involving the knees

Fig. 20.43
Polyarticular juvenile idiopathic arthritis

polyarthritis. About 75% of children are positive for antinuclear antibodies (ANA).

- *Uveitis* is common in this group and affects about 20% of children. Risk factors for uveitis are early-onset of JIA, and positive findings for ANA and HLA-DR5.

b. ***Polyarticular***-onset JIA accounts for a further 20% of cases. It affects girls about three times as often as boys and may commence at any age throughout childhood. The arthritis involves five or more joints, with both small and large joints being involved symmetrically (Fig. 20.43). Systemic features are mild or absent. About 40% of children are positive for ANA.

- *Uveitis* occurs in about 5% of cases.

c. ***Systemic***-onset JIA accounts for about 20% of cases. The disease occurs with equal frequency in boys and girls and may occur at any age throughout childhood. Systemic features include a high remittent fever, transient maculopapular rash, generalized lymphadenopathy, hepatosplenomegaly and serositis. Initially, arthralgia or arthritis may be absent or minimal, and only a minority of patients subsequently develop a progressive polyarthritis. The term '*Still's disease*' is reserved for patients in this subgroup.

- *Uveitis* does not occur.

2. **Treatment** options include physiotherapy, NSAIDs and low-dose methotrexate.
3. **Ophthalmic features.** Chronic anterior uveitis.

Kearns–Sayre syndrome

Kearns–Sayre syndrome is a mitochondrial cytopathy associated with mitochondrial DNA deletions.

1. **Presentation** is in the first to second decades with an insidious onset of bilateral ptosis and limitation of ocular movements in all directions of gaze (progressive external ophthalmoplegia).
2. **Signs**
   - Ataxia and cardiac conduction defects.
   - Fatigue and proximal muscle weakness are common.
   - Deafness, diabetes, short stature and hypoparathyroidism may be present.

3. **Diagnostic tests**. Lumbar puncture shows increased CSF protein concentration (>1 g/l). ECG demonstrates cardiac conduction defects.
4. **Ophthalmic features**. Symmetrical ptosis, external ophthalmoplegia and pigmentary retinopathy.

Fig. 20.44
Lepromatous cutaneous plaques

Fig. 20.45
Lepromatous cutaneous nodules

Leprosy

Leprosy (Hansen disease, hanseniasis) is a chronic granulomatous infection caused by an intracellular acid-fast bacillus, *Mycobacterium leprae*. The exact mode of infection is unknown although the upper respiratory tract appears the most likely portal of entry.

1. **Lepromatous leprosy** is a generalized, multisystem infection with widespread lesions of skin, peripheral nerves, upper respiratory tract, reticuloendothelial system, eyes, bones and testes. Important signs include:
   a. Skin. Erythema nodosum, plaques (Fig. 20.44) and nodules (Fig. 20.45).

Fig. 20.46
Saddle-shaped nose in leprosy

Fig. 20.47
Shortening of digits in leprosy (Courtesy of T. Ffytche)

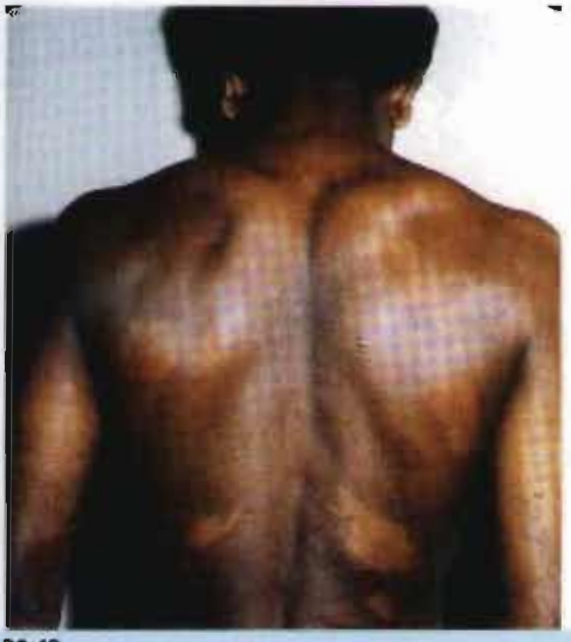

Fig. 20.48
Hypopigmented skin patches in leprosy

b. Nose. Mucosal thickening and saddle-shaped deformity (Fig. 20.46).

c. Neurological. Peripheral neuropathy results in loss of sensory, autonomic and motor function.

- Sensory neuropathy facilitates trauma which may result in shortening of digits (Fig. 20.47) from a multitude of mechanisms.
- Autonomic neuropathy leads to dry, cracked, infection-prone skin; often superimposed on this is secondary bacterial infection, with gross destruction of the tissues.
- Motor neuropathy is exemplified by the 'claw hand' deformity, due to ulnar nerve palsy.

2. **Tuberculoid leprosy** is restricted to the skin and peripheral nerves.
   a. Skin. Annular, anaesthetic, hypopigmented lesions with raised edges (Fig. 20.48).
   b. Nerves. Thickening of cutaneous sensory nerves.
3. **Treatment** is with dapsone, rifampicin and clofazimine.
4. **Ophthalmic features**
   a. Common. Madarosis and lagophthalmos due to seventh nerve palsy. Neurotrophic keratitis due to trigeminal involvement.
   b. Uncommon. Anterior uveitis.

Lyme disease

Lyme disease (borreliosis) is an infection caused by a spirochete, *Borrelia burgdorferi*, transmitted through the bite of a deer tick, *Ixodes ricinus*. Systemic manifestations are complex and are best conceptualized as early and late.

1. **Early** stage presents several days after the bite with a pathognomonic annular expanding skin lesion (erythema chronicum migrans) which may be accompanied by constitutional symptoms and lymphadenopathy. This may last for several weeks and resolve even without treatment. Complications, both neurological (cranial nerve palsies, meningitis) and cardiac (conduction defects, myocarditis), may follow within 3–4 weeks of the initial manifestations.
2. **Late** complications, most commonly chronic arthritis of large joints, may ensue and cause problems for years. Polyneuropathy and chronic acrodermatitis may also occur.
3. **Diagnostic tests** include PCR and ELISA.
4. **Treatment** is with oral doxycycline or intravenous ceftriaxone for neurological involvement.
5. **Ophthalmic features**
   a. Common. Photophobia, pain, periocular oedema and conjunctivitis.
   b. Uncommon. Keratitis, anterior uveitis, intermediate uveitis, optic neuritis, neuroretinitis and ocular motor nerve palsies.
   c. Rare. Peripheral multifocal choroiditis and retinal periphlebitis.

Marfan syndrome

Marfan syndrome is a widespread disorder of connective tissue associated with mutation of the fibrillin gene on chromosome 15q.

1. **Inheritance** is AD with variable expressivity.

Fig. 20.49
Marfan syndrome (see text)

Fig. 20.50
Arachnodactyly in Marfan syndrome

2. Classical signs

a. Musculoskeletal

- Tall, thin stature, scoliosis, sternal deformity (prominence or depression).
- Disproportionately long limbs compared with the trunk (arm span > height) (Fig. 20.49).
- Long spider-like fingers (arachnodactyly) and mild joint hypermobility (Fig. 20.50).
- A narrow and high-arched (gothic) palate (Fig. 20.51).
- Muscular underdevelopment and predisposition to hernias.

b. Cardiovascular

- Dilatation of the ascending aorta leading to aortic incompetence and heart failure (Fig. 20.52).
- Mitral valve disease and aortic dissection.

c. Skin. Striae, fragility and easy bruising.

3. Ophthalmic features

a. Common. Ectopia lentis, hypoplasia of dilator pupillae, angle anomaly, myopia and retinal detachment.

b. Uncommon. Microspherophakia, keratoconus and cornea plana.

c. Rare. Megalocornea.

Fig. 20.51
High-arched palate in Marfan syndrome

Multiple sclerosis

Multiple sclerosis (MS) is an idiopathic, remitting, demyelinating disease involving white matter within the CNS.

1. Presentation is in the third to fourth decades with remitting/relapsing involvement occurring at random frequency and of unpredictable duration.

2. Signs

a. Spinal cord. Weakness, stiffness, sphincter disturbance and sensory loss with a 'trouser-like' distribution.

b. Brain stem. Diplopia, nystagmus, dysarthria and dysphagia.

c. Cerebral hemisphere. Hemiparesis, hemianopia and dysphasia.

d. Psychological. Intellectual decline, depression, euphoria and dementia.

3. Transient features include Lhermitte sign (electrical sensation on neck flexion), dysarthria–dysequilibrium–diplopia syndrome and Uhthoff phenomenon (sudden worsening of vision or other symptoms on exercise or increase in body temperature).

4. Diagnostic tests

a. Lumbar puncture shows leucocytosis, IgG level > 15% of total protein and oligoclonal bands on protein electrophoresis.

b. MRI shows ovoid periventricular and corpus callosum plaques with their long axes perpendicular to the ventricular margins (*see* Figs 18.24 and 18.25). Acute demyelination plaques may be highlighted with gadolinium on T1-weighted scans.

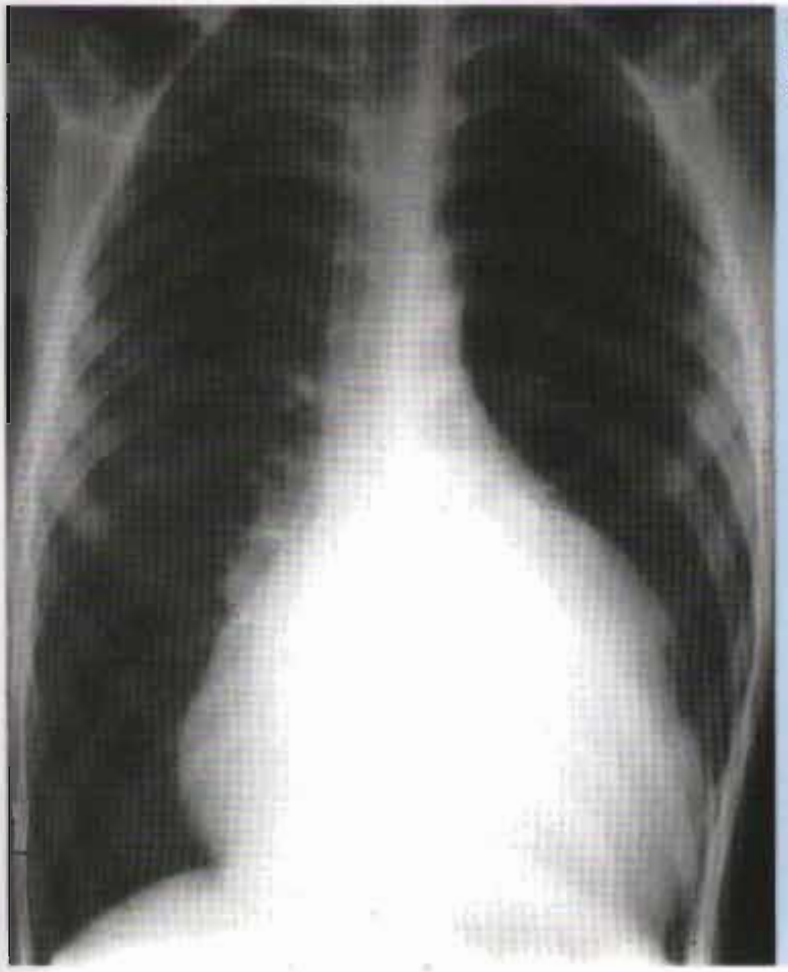

Fig. 20.52
Elongated chest and enlarged heart in Marfan syndrome
(Courtesy of S. Ghiacy)

5. **Treatment** options include systemic steroids and interferon beta-1a.
6. **Ophthalmic features**
   a. *Common*. Optic neuritis (usually retrobulbar), internuclear ophthalmoplegia and nystagmus.
   b. *Uncommon*. Skew deviation, ocular motor nerve palsies and hemianopia.
   c. *Rare*. Intermediate uveitis and retinal periphlebitis.

Myasthenia gravis

Myasthenia gravis is an autoimmune disease in which antibodies mediate damage and destruction of acetylcholine receptors in striated muscle. The resultant impairment of neuromuscular conduction causes weakness and fatiguability of skeletal musculature but not of cardiac and involuntary muscles. The disease affects females twice as commonly as males. Myasthenia may be (a) *ocular*, (b) *bulbar* or (c) *generalized*.

1. **Presentation** is most commonly in the third decade, but may be at any time after the first year of life, most frequently with ptosis or diplopia. Patients with generalized involvement then develop painless fatigue often brought on by exercise, which may be worse towards the end of the day and provoked by infection or stress.
2. **Signs.** The most important feature is fatiguability, affecting musculature of the limbs and that involved in facial expression, ocular movements, mastication and speech.
   a. *Peripheral*. Weakness, particularly of the arms and proximal muscles of the legs. Permanent myopathic wasting may occur in long-standing cases.
   b. *Facial*. Lack of expression (myopathic facies) and ptosis.
   c. *Bulbar*. Difficulties with swallowing (dysphagia), speaking (dysarthria) and chewing.
   d. *Respiratory*. Difficulty with breathing is rare but serious.
3. **Diagnostic tests**
   - Positive edrophonium test (*see* Chapter 18).
   - Raised serum acetylcholine receptor antibody levels.
   - Thoracic CT (Fig. 20.53) or MRI to detect thymoma which is present in 10% of patients. Patients under the age of 40 years without thymoma generally have a hyperplastic thymus; in older patients the thymus is usually normal (atrophic).
4. **Treatment** options include anticholinesterase drugs (pyridostigmine, neostigmine), steroids, immunosuppressive drugs (azathioprine, cyclosporin), plasma exchange, intravenous immunoglobulins and thymectomy. Patients with pure ocular myasthenia are usually not helped by thymectomy.
5. **Ophthalmic features**
   a. *Common*. Ptosis and diplopia. Inability to maintain upgaze. Cogan 'lid-twitch' sign. Weakness of orbicularis oculi with compromised lid closure.
   b. *Uncommon*. Pseudo-internuclear ophthalmoplegia.

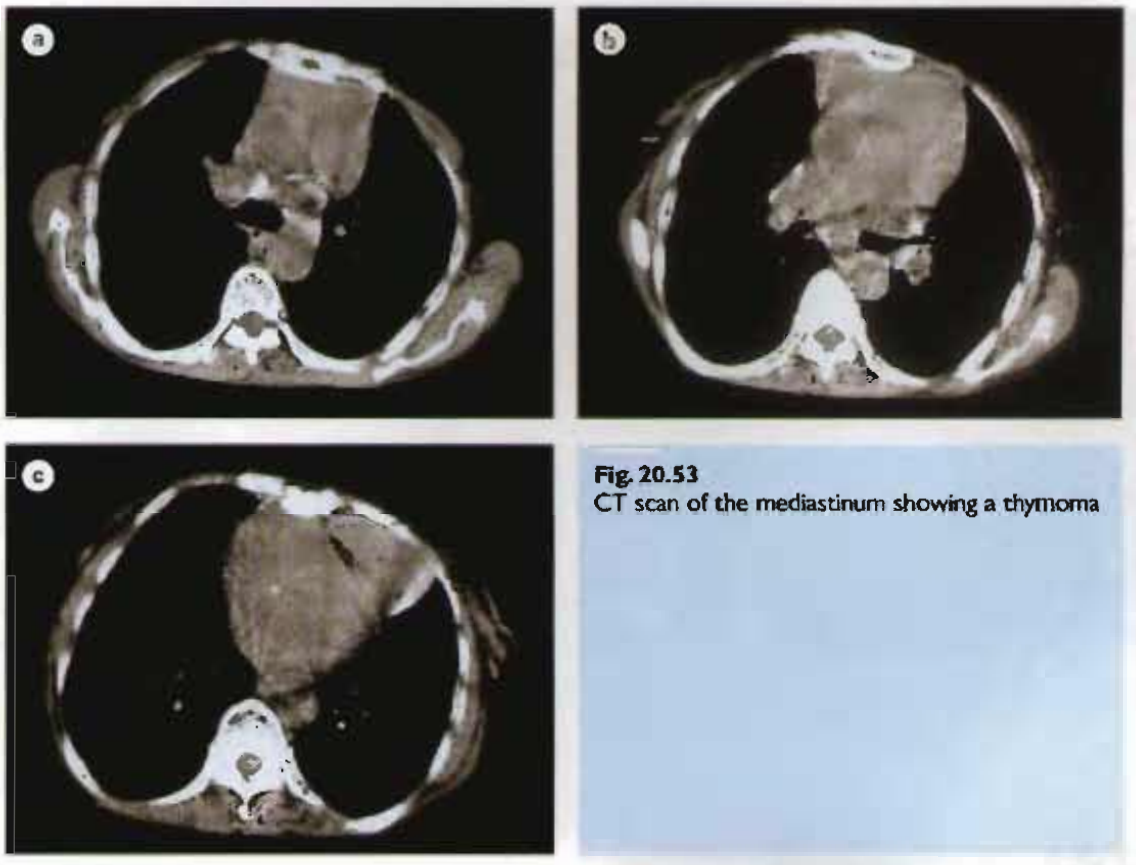

Fig. 20.53
CT scan of the mediastinum showing a thymoma

NB: Bizarre defects of ocular motility may occur; myasthenia should therefore be considered in the differential diagnosis of any ocular motility disorder that does not fit with a recognized pattern.

Myotonic dystrophy

Myotonic dystrophy (dystrophia myotonica, Steinert disease) is characterized by delayed muscular relaxation after cessation of voluntary effort (myotonia). The gene locus is on 19q13.3.

1. **Inheritance** is AD.
2. **Presentation** is in the third to sixth decades with weakness of the hands and difficulty in walking. Successive generations exhibit progressively earlier onset and greater severity of disease, a phenomenon termed 'anticipation'.
3. **Signs**
   a. *Peripheral.* Difficulty in releasing grip (Fig. 20.54), muscle wasting and weakness.
   b. *Central.* Mournful facial expression (Fig. 20.55) caused by bilateral facial wasting with hollow cheeks and slurred speech from involvement of the tongue and pharyngeal muscles.
   c. *Other.* Frontal baldness in males (Fig. 20.56), hypogonadism, mild endocrine abnormalities, cardiomyopathy, pulmonary disease, intellectual deterioration and bone changes.
4. **Diagnostic tests.** Electromyography shows myotonic and myopathic potentials, and serum creatine kinase is elevated.

Fig. 20.54
Difficulty in relaxation of grip in myotonic dystrophy

5. **Treatment** involves exercise and prevention of contractures.
6. **Ophthalmic features**
   a. *Common.* Early-onset stellate cataracts and ptosis.
   b. *Uncommon.* External ophthalmoplegia, pupillary light-near dissociation, mild pigmentary retinopathy and low intraocular pressure.

Neurofibromatosis-1

Neurofibromatosis-1 (NF-1, von Recklinghausen disease) is a phacomatosis that primarily affects cell growth of neural tissues. The gene locus is on 17q11.

Fig. 20.55
Mournful facial expression in myotonic dystrophy

Fig. 20.56
Mournful facial expression, frontal balding and right cataract in myotonic dystrophy

Fig. 20.57
Mild macrocephaly in NF-1

Fig. 20.58
Right facial hemiatrophy and fibroma mollusca in NF-1

1. **Inheritance** is AD with irregular penetrance and variable expressivity.
2. **Signs**
   a. ***Neural tumours*** in the CNS and in cranial, peripheral and sympathetic nerves.
   b. ***Skeletal.*** Short stature, mild macrocephaly (enlarged head) (Fig. 20.57), facial hemiatrophy (Fig. 20.58), absence of the great wing of the sphenoid bone (*see* Fig. 18.117), scoliosis and thinning of long bone cortex.
   c. ***Skin***
      - Café-au-lait spots are flat, light-brown patches (Figs 20.59c and 20.60). They appear during the first year of life and increase in size and number throughout childhood; teenagers and adults invariably have more than six.
      - Axillary freckles usually become obvious around the age of 10 years and are pathognomonic.
      - Fibroma mollusca are pedunculated, flabby nodules (Fig. 20.61) which are often widely distributed over the body (Fig. 20.62 and *see* Fig. 20.59b). They appear at about puberty and increase in number throughout life.

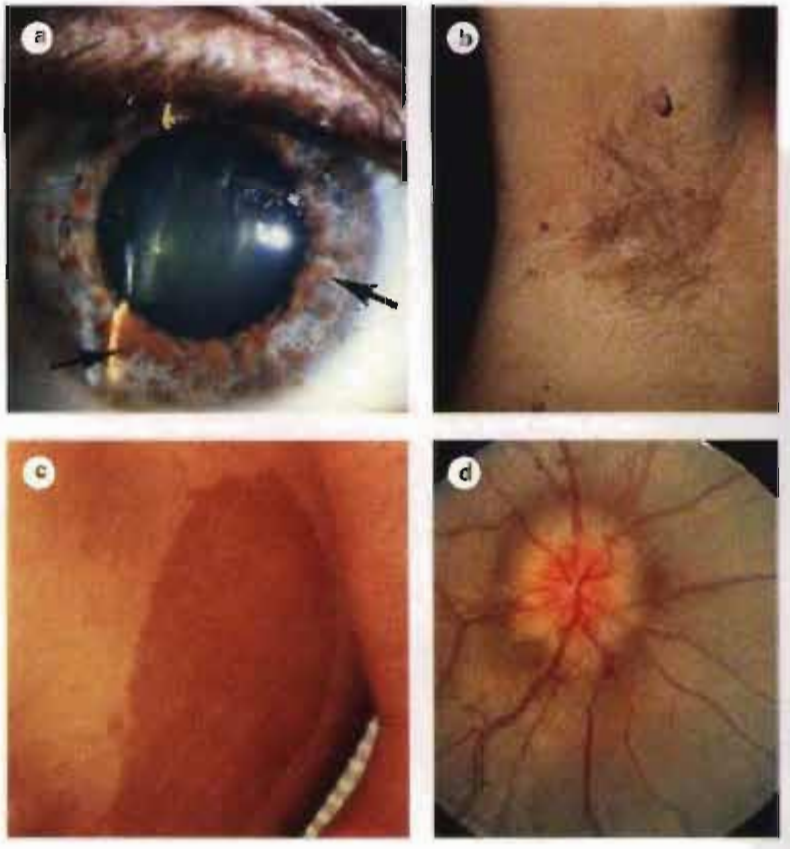

Fig. 20.59
NF-1. (a) Lisch nodules; (b) fibroma mollusca; (c) café-au-lait spot; (d) optic disc oedema due to optic nerve glioma (Courtesy of Wilmer Institute)

Fig. 20.60
Café-au-lait spots in NF-1

Fig. 20.61
Fibroma mollusca in NF-1

- Plexiform neurofibromas may be associated with pigmentation and overgrowth of the overlying soft tissues (Fig. 20.63 and Fig. 20.64). They may be present at birth or appear during childhood and may occur anywhere on the body. Rarely they may involve the face and cause disfigurement (Fig. 20.65).

3. **Associations** include malignancies, hypertension and mental handicap.
4. **Ophthalmic features**
   a. ***Common***. Eyelid neurofibromas and Lisch nodules (*see* Fig. 20.59a).
   b. ***Uncommon***. Optic nerve glioma (*see* Fig. 20.59d), ectropion uveae and glaucoma.
   c. ***Rare***. Other neural orbital tumours, spheno-orbital encephalocele, prominent corneal nerves, iris mammillations, choroidal naevi, choroidal melanomas and retinal astrocytomas.

Neurofibromatosis-2

Neurofibromatosis-2 (NF-2) is less common than NF-1, with the gene locus at 22q12.

Fig. 20.62
Extensive fibroma mollusca in NF-1

Fig. 20.63
Plexiform fibroma of the right palm in NF-1

Fig. 20.64
Plexiform neurofibroma and soft tissue hypertrophy in NF-1

Fig. 20.65
Extensive facial plexiform neurofibroma and soft tissue hypertrophy in NF-1

1. **Inheritance** is AD.
2. **Diagnostic criteria**
   a. ***Bilateral acoustic neuromas*** which usually present in the late teens or early twenties with hearing loss, tinnitus or imbalance. Most acoustic neuromas are schwannomas arising from the vestibular nerve. In young patients tumour growth is invariably fast, whereas in older patients the lesion may be either slow- or fast-growing. Recent advances in microsurgical techniques have significantly improved the results of surgery. The gamma-knife (stereotactic radiotherapy) provides a therapeutic option.
   b. ***A patient with a first-degree relative with NF-2*** who also has either a unilateral acoustic neuroma or two of the following: neurofibroma, meningioma, glioma, schwannoma or juvenile cataract.
3. **Ophthalmic features**
   a. ***Common***. Early-onset cataract.
   b. ***Uncommon***. Ophthalmoplegia, combined hamartomas of the RPE and retina and epiretinal membranes.

Polyarteritis nodosa

Polyarteritis nodosa (PAN) is an idiopathic, potentially lethal, collagen vascular disease affecting medium-sized and small arteries, with frequent aneurysm formation. It is three times more common in males than in females.

1. **Presentation** is in the third to sixth decades with tachycardia, myalgia, arthralgia, fever and weight loss.

Fig. 20.66
Cutaneous vasculitis

Fig. 20.67
Skin papules in pseudoxanthoma elasticum

2. **Signs**
   a. *Skin*. Purpura and easy bruising, vasculitis (Fig. 20.66), infarcts, gangrene and livedo reticularis.
   b. *Muscles*. Weakness and tenderness.
3. **Complications**
   - Renal involvement and hypertension.
   - Coronary arteritis which may lead to heart failure and myocardial infarction.
   - Gastrointestinal bleeding or an acute abdominal crisis.
   - Stroke or multifocal neuropathy.
4. **Diagnostic tests** show eosinophilia, hypergammaglobulinaemia and necrotizing lesions on skin biopsy.
5. **Treatment** is with systemic steroids and immunosuppressive agents.
6. **Ophthalmic features**
   a. *Common*. Peripheral ulcerative keratitis and scleritis.
   b. *Rare*. Orbital pseudo-tumour and occlusive retinal periarteritis.

Fig. 20.68
Loose axillary skin in pseudoxanthoma elasticum

Pseudoxanthoma elasticum

Pseudoxanthoma elasticum is a hereditary disorder of elastin. There are four distinctive types, in which ocular manifestations are common but of variable severity.

1. **Dominant type 1**
   - Small, yellowish skin papules arranged in linear or reticulate plaques most commonly on the neck (Fig. 20.67), axillae (Fig. 20.68), antecubital fossae, groins and paraumbilical area (Fig. 20.69). Involved skin becomes progressively loose.
   - Thin, delicate skin which bruises easily.
   - Accelerated atherosclerosis and mitral valve disease.
   - Severe angioid streaks (Groenblad–Strandberg syndrome).
2. **Dominant type 2**
   - Fewer and flatter skin papules than in dominant type 1.
   - Skin hyperelasticity and high-arched palate.
   - Mild angioid streaks and blue sclera.
3. **Recessive type 1**
   - Skin changes are similar to dominant type 1.

Fig. 20.69
Pseudoxanthoma elasticum involving the paraumbilical area

- Mild vascular disease but frequent gastrointestinal bleeding.
- Mild angioid streaks.

4. **Recessive type 2**
   - Severe and generalized skin changes.
   - No systemic complications.
   - Angioid streaks.

Psoriatic arthritis

Psoriatic arthritis is a spondarthropathy which develops in about 7% of patients with psoriasis. The disease affects both sexes equally and is associated with an increased prevalence of HLA-B27 and HLA-B17.

1. **Presentation** is in the third to fourth decades.
2. **Signs**
   a. Skin
   - Plaque psoriasis (most common): well-demarcated, salmon-pink areas covered with thick, silvery plaques, commonly seen on extensor surfaces and the scalp (Fig. 20.70).
   - Flexural psoriasis: non-scaly pink lesions, commonly affecting the groin and perineum.
   - Pustular psoriasis is characterized by pustular lesions on the palms and soles in association with scaling and erythema.
   - Erythrodermic psoriasis is characterized by severe erythema and scaling, often with pustule formation, involving the trunk and limbs.

   b. Arthritis may take one of the following patterns:
   - Asymmetrical involvement of the distal interphalangeal joints which may give rise to sausage-shaped deformities (Fig. 20.71).
   - Pauciarticular peripheral involvement.
   - Symmetrical peripheral involvement similar to rheumatoid arthritis.
   - Arthritis mutilans affecting a few digits is rare.
   - Associated ankylosing spondylitis.

   c. Nail dystrophy. Pitting, transverse depression and onycholysis (Fig. 20.72).

Fig. 20.70

Fig. 20.71
Sausage-like deformities of digits in psoriatic arthritis

Fig. 20.72
Psoriatic nail dystrophy

3. **Treatment**. NSAIDs, intra-articular steroids; severe disease may require cytotoxic drugs.
4. **Ophthalmic features**
   a. Uncommon. Acute anterior uveitis.
   b. Rare. Conjunctivitis, keratitis and keratoconjunctivitis sicca.

Reiter syndrome

Reiter syndrome (reactive arthritis) is a spondarthropathy which typically affects young males and is characterized by the triad of urethritis, conjunctivitis and arthritis. About 70% of patients are positive for HLA-B27.

1. **Presentation** is in the third to fourth decades with urethritis, conjunctivitis and arthritis, occurring within a short period of each other, classically following dysentery or sexual intercourse. Presentetion may, however, be insidious.
2. **Signs**
   a. Arthritis. Asymmetrical involvement of the knees or ankles is most common and may be migratory. The shoulders, wrists, elbows, hips, spine and sacro-iliac

Fig. 20.73
Achilles tenosynovitis in Reiter syndrome

Fig. 20.74
Keratoderma blenorrhagica in Reiter syndrome

Fig. 20.75
Circinate balanitis and urethral discharge in Reiter syndrome

*b. **Enthesopathy**.* Plantar fasciitis, Achilles tendonitis (Fig. 20.73), bursitis and calcaneal periostitis. Reactive bone formation in the latter may result in a calcaneal spur.

*c. **Mucocutaneous**.* Painless mouth ulceration, keratoderma blenorrhagica involving the palms and soles (Fig. 20.74), circinate balanitis (Fig. 20.75) and nail dystrophy.

*d. **Genitourinary**.* Cystitis, cervicitis, prostatitis, epididymitis and orchitis.

*e. **Aortic incompetence*** is uncommon.

3. **Treatment** is with NSAIDs.
4. **Ophthalmic features**
   *a. **Common**.* Conjunctivitis and acute anterior uveitis.
   *b. **Uncommon**.* Corneal infiltrates.

Rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune systemic disease characterized by a symmetrical, destructive, deforming, inflammatory polyarthropathy, in association with a spectrum of extra-articular manifestations and circulating antiglobulin antibodies, termed rheumatoid factors. It affects females more commonly than males.

1. **Presentation** is in the fourth decade and occasionally in childhood (juvenile rheumatoid arthritis). The disease is characterized by exacerbations alternating with phases of quiescence.
2. **Signs**
   a. Arthritis
   - Symmetrical involvement of the small joints of the hands and feet. Inflammation typically involves the proximal interphalangeal and spares the distal interphalangeal joints. The metacarpophalangeal and wrist joints are also commonly involved.
   - Less frequent involvement of the shoulders, elbows, hips and cervical spine.
   - Joint instability secondary to chronic inflammation may result in subluxation and deformities, such as ulnar deviation of the metacarpophalangeal joints (Fig. 20.76).

   b. Skin. Raynaud phenomenon, vasculitis (Fig. 20.77), subcutaneous nodules (Fig. 20.78) and occasionally pyoderma gangrenosum.

Fig. 20.76
Ulnar deformity of the right hand in rheumatoid arthritis

Fig. 20.77
Cutaneous vasculitis in rheumatoid arthritis

Fig. 20.78
Rheumatoid nodules

3. **Complications**
   - Pulmonary nodules and fibrosis.
   - Multifocal neuropathy.
   - Septic arthritis.
   - Secondary amyloidosis.
   - Carpal tunnel syndrome.
4. **Treatment** options include NSAIDs, gold salts, D-penicillamine, hydroxychloroquine, sulphasalazine, steroids and cytotoxic agents.
5. **Ophthalmic features**
   a. Common. Keratoconjunctivitis sicca (secondary Sjögren syndrome).
   b. Uncommon. Scleritis and peripheral ulcerative keratitis.
   c. Rare. Acquired superior oblique tendon sheath syndrome.

Rosacea

Rosacea is an idiopathic skin disease which principally affects the glabella, cheeks, nose and chin.

1. **Presentation** is in adult life with itching and flushing of facial skin, often precipitated by alcohol or spicy food.
2. **Signs**
   - *Stage 1.* Erythema progressing to telangiectasia (Fig. 20.79).

Fig. 20.79
Acne rosacea—stage 1 (see text)

Fig. 20.80
Severe acne rosacea—stage 2 (see text)

   - *Stage 2.* Papules and pustules (Fig. 20.80).
   - *Stage 3.* Inflammatory nodules, sebaceous gland hyperplasia (Fig. 20.81) and rhinophyma.
3. **Treatment** is with topical metronidazole gel and systemic tetracycline.
4. **Ophthalmic features**
   a. Common. Chronic posterior blepharitis and recurrent meibomian cysts.
   b. Uncommon. Conjunctivitis and peripheral keratitis.

Sarcoidosis

Sarcoidosis is an idiopathic multi-system granulomatous inflammatory disorder, more common in patients of African descent than in Caucasians.

1. **Presentation**
   a. Acute-onset sarcoidosis typically occurs during the third decade:
   - Löfgren syndrome is characterized by fever, erythema nodosum (Fig. 20.82), bilateral hilar lymphadenopathy (Fig. 20.83) and frequently arthralgia.

Fig. 20.81
Acne rosacea—stage 3 (see *text*)

Fig. 20.83
Bilateral hilar lymphadenopathy in acute sarcoidosis

Fig. 20.82
Erythema nodosum

Fig. 20.84
Facial palsy and lupus pernio involving the nose in sarcoidosis

- Heerfordt syndrome (uveoparotid fever) is characterized by fever, parotid gland enlargement and uveitis.
- Seventh nerve palsy (Fig. 20.84) may be associated with other neurological features.

b. Insidious-onset sarcoidosis typically occurs during the fifth decade with fatigue, dyspnoea and arthralgia.

2. Signs

a. Pulmonary involvement is present in 90% of patients and varies in severity from asymptomatic bilateral hilar lymphadenopathy to progressive pulmonary fibrosis and bronchiectasis.

b. Skin. Erythema nodosum, granulomata (Fig. 20.85) and lupus pernio (Fig. 20.86). The latter is characterized by indurated, purple-blue lesions.

c. Neurological. Cranial nerve palsies (particularly facial), meningeal infiltration, and intracranial and intraspinal granulomas.

d. Other. Reticuloendothelial, hepatic, renal, bone and cardiac involvement.

3. Diagnostic tests

a. Chest radiographs are abnormal in 90% of cases.

b. Biopsy

- Of the lungs gives the greatest yield (90%).
- Of the conjunctiva is positive in about 70% of patients.
- Of lacrimal glands is positive in 25% of unenlarged and 75% of enlarged glands.

Fig. 20.85
Cutaneous sarcoid granulomas

Fig. 20.86
Lupus pernio

c. ***Serum angiotensin-converting enzyme*** (ACE) is elevated in patients with active disease but normal during remissions. The normal serum level in adults is 32.1 ± 8.5 IU. In patients with suspected neurosarcoid ACE can be measured in the cerebrospinal fluid. ACE may also be elevated in other conditions such as tuberculosis, lymphoma and asbestosis.

d. ***Bronchioalveolar lavage*** shows a raised proportion of activated T-helper lymphocytes.

e. ***Calcium assay*** may be useful because calcium metabolism is abnormal. Hypercalciuria is common but hypercalcaemia is unusual.

f. ***Gallium-67 scanning*** of the head, neck and thorax frequently shows increased uptake.

g. ***Pulmonary function tests*** reveal a restrictive lung defect with reduced total lung capacity.

4. **Treatment** options include NSAIDs, steroids and low-dose cytotoxic agents.
5. **Ophthalmic features**
   a. ***Common***. Conjunctival granulomas, anterior uveitis, posterior uveitis and retinal periphlebitis.
   b. ***Uncommon***. Keratoconjunctivitis sicca and intermediate uveitis.
   c. ***Rare***. Fundus granulomas, retinal and disc neovascularization, and papilloedema.

Sjögren syndrome

Sjögren syndrome is characterized by autoimmune inflammation and destruction of lacrimal and salivary glands. The condition is classified as primary when it exists in isolation, and secondary when associated with other diseases such as rheumatoid arthritis and systemic lupus erythematosus. Primary Sjögren syndrome affects females more commonly than males.

1. **Presentation** is in adult life with grittiness of the eyes and dryness of the mouth.
2. **Signs**
   - Enlargement of the salivary glands with diminished salivary flow rate and a dry fissured tongue (Fig. 20.87).
   - Dry nasal passages, diminished vaginal secretions and dyspareunia.
   - Raynaud phenomenon and cutaneous vasculitis.
3. **Complications**
   - Reflux oesophagitis and gastritis.
   - Malabsorption due to pancreatic failure.
   - Pulmonary disease, renal disease and polyneuropathy.
4. **Diagnostic tests**. Serum autoantibodies, Schirmer test and biopsy of minor salivary glands.
5. **Treatment** options include systemic steroids and cytotoxic agents.
6. **Ophthalmic features**
   a. ***Common***. Keratoconjunctivitis sicca.
   b. ***Rare***. Adie pupil.

Fig. 20.87
Dry fissured tongue in Sjögren syndrome

Stevens–Johnson syndrome

Stevens–Johnson syndrome (erythema multiforme major) is an acute, serious but generally self-limiting mucocutaneous, blistering disease, primarily occurring in healthy young individuals. The most frequent precipitating factors of this severe type III hypersensitivity reaction are certain drugs (e.g. sulphonamides, tetracycline, NSAIDs and penicillin), infections with *Mycoplasma pneumoniae* and herpes simplex, and radiotherapy for malignancy. In over 50% of cases there is no apparent cause. The underlying pathology is a generalized vasculitis secondary to deposition of circulating immune complexes.

1. **Presentation** is in the third to fifth decades with constitutional symptoms followed by mucocutaneous lesions.
2. **Signs**
   a. Mucosa
   - Oral and nasal blisters, which rupture forming erosions, are universal; the lips exhibit haemorrhagic crusting (Fig. 20.88).
   - Genital involvement may occur (Fig. 20.89).

Fig. 20.88
Haemorrhagic crusting in Stevens–Johnson syndrome

Fig. 20.89
Involvement of the glans penis in Stevens–Johnson syndrome

   b. Skin
   - A generalized erythematous papular rash, which evolves into 'target' lesions, consisting of erythematous centres surrounded by pale areas, in turn encircled by erythematous rings (Fig. 20.90).
   - Blisters are usually transient but may be widespread and associated with haemorrhage and necrosis (Fig. 20.91).
   - Healing occurs within 1–4 weeks, sometimes leaving a scar.
3. **Treatment** is with systemic steroids; aciclovir may be used if herpes simplex is suspected as the causative agent.
4. **Ophthalmic features**
   a. Common. Transient membranous conjunctivitis.
   b. Uncommon. Cicatricial conjunctivitis.

Sturge–Weber syndrome

Sturge–Weber syndrome (encephalotrigeminal angiomatosis) is a sporadic phacomatosis.

Fig. 20.90
Target lesion in Stevens–Johnson syndrome

Fig. 20.91
Haemorrhagic vesiculobullous skin lesions and area of necrosis in Stevens–Johnson syndrome

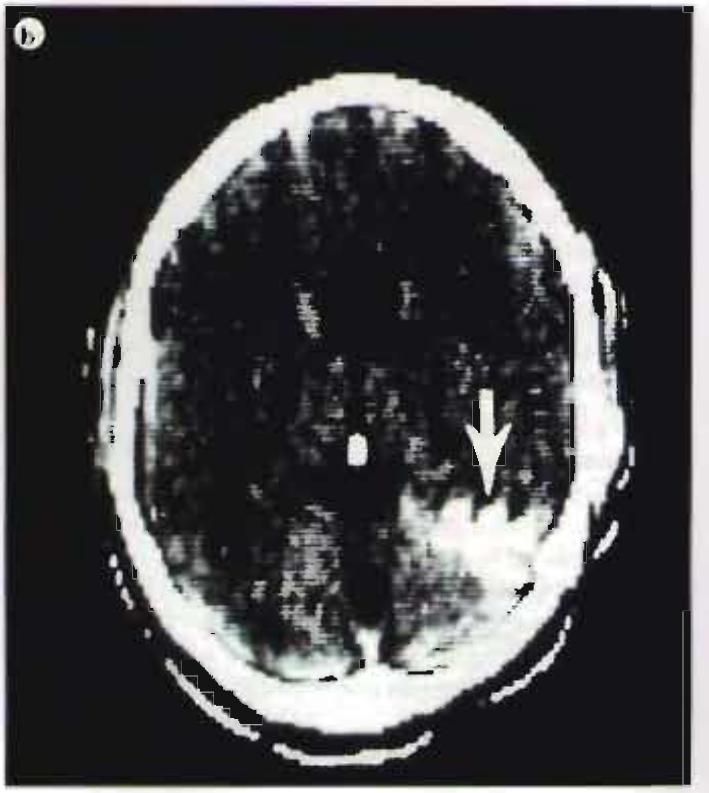

Fig. 20.92
Sturge–Weber syndrome. (a) Naevus flammeus; (b) axial CT scan showing a meningeal haemangioma (Courtesy of Wilmer Institute)

1. **Classification**
   - *a. Trisystem* involves the face, leptomeninges and eyes.
   - *b. Bisystem* involves the face and eyes or the face and leptomeninges.
2. **Presentation** is at birth.
3. **Signs**
   - Facial naevus flammeus (port-wine stain), extending over an area corresponding to the distribution of one or more branches of the trigeminal nerve (Fig. 20.92a).
   - Ipsilateral parietal or occipital leptomeningeal haemangioma may cause contralateral focal or generalized seizures, hemiparesis and hemianopia.
   - Mental retardation is frequent.
4. **Diagnostic tests.** Plain radiographs may show 'tramline markings' of cerebral calcification. The haemangioma will also be apparent on CT (Fig. 20.92b) and MRI.
5. **Ophthalmic features**
   - *a. Common.* Ipsilateral glaucoma and diffuse choroidal haemangioma.
   - *b. Uncommon.* Ipsilateral episcleral haemangioma.
   - *c. Rare.* Heterochromia iridis.

Syphilis: acquired

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*.

1. **Stages**
   - *a. Primary* stage occurs after an incubation period commonly lasting 2–4 weeks and is characterized by a painless ulcer (chancre) at the site of inoculation (usually genitalia) and associated regional lymphadenopathy.
   - *b. Secondary* stage usually occurs 6–8 weeks after the chancre and is characterized by:
     - Generalized lymphadenopathy with mild or absent constitutional symptoms.

Fig. 20.93
Rash in secondary syphilis

Fig. 20.94
Rash in secondary syphilis

- Symmetrical maculopapular rash on the trunk (Fig. 20.93), palms and soles (Fig. 20.94).
- Condylomata lata in the anal region.
- Mucous patches in the mouth, pharynx and genitalia consisting of painless greyish-white circular erosions ('snail-track ulcers').
- Meningitis, nephritis and hepatitis may occur.
- Secondary syphilis resolves in a few months, even without treatment.

c. Latent stage follows resolution of secondary syphilis, may last for years and can be detected only by serological tests.

d. Tertiary stage occurs in about 40% of untreated cases and is characterized by:

- Cardiovascular manifestations: aortitis with aneurysm formation and aortic regurgitation.
- Neurosyphilis: tabes dorsalis, Charcot joints and general paralysis of the insane.
- Gummata in various organs.

2. Diagnostic tests

a. VDRL (Venereal Disease Research Laboratory). The titres reflect disease activity. It becomes positive during the primary stage and may become negative if treatment is given early.

b. FTA-ABS (fluorescent treponemal antibody absorption) is specific for treponema antibodies but is not titratable.

c. MHA-TP (microhaemagglutination assay with *Treponema pallidum* antigen) is specific for treponema antibodies but may be negative in early primary syphilis.

3. Treatment may be with procaine penicillin, doxycycline or erythromycin.

4. Ophthalmic features

a. Common. Madarosis and keratitis.

b. Uncommon. Anterior uveitis, chorioretinitis, periarteritis and neuroretinitis.

c. Rare. Optic neuritis, Argyll Robertson pupils and ocular motor nerve palsies.

Syphilis: congenital

Transplacentally acquired infection may result in stillbirth, stigmata of congenital syphilis or be subclinical.

1. Signs

a. Early

- Rhinitis and failure to thrive.
- Maculopapular rash, especially on the buttocks and thighs, and mucosal ulcers.
- Fissures around the lips, nares and anus.
- Pneumonia, hepatosplenomegaly, lymphadenopathy and jaundice.

b. Late

- Sensorineural deafness.
- Frontal bossing, short maxilla, prognathism, high-arched palate and saddle-shaped nose.
- Malformed incisors (Hutchinson teeth) and mulberry molars.

2. Ophthalmic features

a. Common. Anterior uveitis and interstitial keratitis in early cases.

b. Uncommon. Pigmentary retinopathy in late cases.

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is an autoimmune, non-organ-specific connective tissue disease characterized by numerous autoantibodies and circulating immune complexes, which mediate widespread vasculitis and tissue damage. It predominantly affects young females.

1. Presentation is in the third to fifth decades with fatigability without specific organ involvement. Alternatively, the disease may present with symmetrical arthralgia.

2. Signs

a. Mucocutaneous. 'Butterfly' facial rash (Fig. 20.95), discoid rash (Fig. 20.96), vasculitis, telangiectasia, photosensitivity, alopecia, oral ulceration and Raynaud phenomenon.

b. Musculoskeletal. Arthritis, myositis and tendonitis.

c. Renal. Glomerulonephritis.

d. Cardiovascular. Pericarditis, endocarditis, myocarditis, and arterial and venous occlusions.

e. Pulmonary. Pleurisy, atelectasis and 'shrinking lungs'.

f. Haemopoietic. Anaemia, thrombocytopenia, lymphopenia and leucopenia.

g. Reticuloendothelial. Splenomegaly and lymphadenopathy.

h. Neurological. Polyneuritis, cranial nerve palsies, spinal cord lesions, epilepsy, stroke and psychosis.

3. Diagnostic tests

- The ESR is raised, but C-reactive protein is usually not.

Fig. 20.95
'Butterfly' rash in systemic lupus erythematosus

Fig. 20.96
Discoid lupus

- A variety of autoantibodies including lupus anticoagulant, antiphospholipid and antinuclear may be present.

4. **Treatment** options include antimalarials, NSAIDs, steroids and cytotoxic agents.
5. **Ophthalmic features**
   - *a. Common*. Madarosis and keratoconjunctivitis sicca.
   - *b. Uncommon*. Peripheral ulcerative keratitis.
   - *c. Rare*. Scleritis, retinal vasculitis and optic neuropathy.

Systemic sclerosis

Systemic sclerosis is an idiopathic, chronic, connective tissue disease affecting the skin (scleroderma) and internal organs, occurring most commonly in females under the age of 50. The risk of internal organ involvement is proportional to the extent of skin involvement. Systemic sclerosis may be (a) *limited*, (b) *diffuse*, (c) *sine scleroderma* and (d) *overlap* with other autoimmune diseases.

1. **Presentation** is in the fourth to sixth decades with Raynaud phenomenon.
2. **Signs**
   - *a. Skin*
     - Tightening and thickening on hands, feet, face and trunk (Fig. 20.97) gives rise to a waxy appearance.
     - Subcutaneous fibrosis causes binding-down of skin, tapering of the fingers with loss of pulps (sclerodactyly) (Fig. 20.98) and subcutaneous deposition of calcium (calcinosis).
     - A typical facial appearance characterized by a fixed expression, restrictive movements of the lips and 'beaking' of the nose often develops.
   - *b. Organs*
     - Oesophageal dysmobility.
     - Heart, lung and kidney disease.
     - Mild arthritis and myositis.
3. **Diagnostic tests**. Positive serum antinuclear and other autoantibodies; skin biopsy.
4. **Treatment** is unsatisfactory.
5. **Ophthalmic features**
   - *a. Common*. Eyelid tightening and telangiectasia.
   - *b. Uncommon*. Keratoconjunctivitis sicca.

Fig. 20.97
Scleroderma involving abdominal skin

Fig. 20.98
Sclerodactyly

Fig. 20.99
Goitre in hyperthyroidism

c. Rare. Conjunctival forniceal shortening and vascular changes, nodular episcleritis, scleral pits, retinal cotton wool spots and patches of choroidal non-perfusion seen only on fluorescein angiography.

Thyrotoxicosis

Thyrotoxicosis (hyperthyroidism) is a clinical condition involving excessive secretion of thyroid hormones. Graves disease, the most common subtype of hyperthyroidism, is an autoimmune disorder in which IgG antibodies bind to thyroid-stimulating hormone (TSH) receptors in the thyroid gland and stimulate secretion of thyroid hormones. It is commoner in females and may be associated with other autoimmune disorders.

1. **Presentation** is in the third to fourth decades with weight loss despite good appetite, increased bowel frequency, sweating, heat intolerance, nervousness, irritability, palpitations, weakness and fatigue.
2. **Signs**
   a. External
   - Diffuse thyroid enlargement (Fig. 20.99), fine hand tremor, palmar erythema, and warm and sweaty skin.
   - Finger clubbing (thyroid acropachy) (Fig. 20.100) and onycholysis (Plummer nails).
   - Alopecia, vitiligo (Fig. 20.101) and pretibial myxoedema (Fig. 20.102).
     - Myopathic proximal muscle weakness but brisk tendon reflexes.

   b. Cardiovascular
   - Sinus tachycardia, atrial fibrillation and premature ventricular beats.
   - High-output heart failure.
3. **Diagnostic tests.** Abnormal thyroid function: serum T_3, T_4, TSH, thyroxine-binding globulin (TBG) and thyroid-stimulating immunoglobulin (TSI).
4. **Treatment** options include carbimazole, propylthiouracil, propranolol, radioactive iodine and partial thyroidectomy.

Fig. 20.100
Thyroid acropachy

Fig. 20.101
Vitiligo

5. **Ophthalmic features**
   a. Common. Lid retraction, chemosis and proptosis.
   b. Uncommon. Superior limbic keratoconjunctivitis keratoconjunctivitis sicca and diplopia.
   c. Rare. Optic neuropathy and choroidal folds.

Fig. 20.102
Pretibial myxoedema

Fig. 20.103
Tuberculosis involving the cervical lymph glands

Fig. 20.104
Tuberculous involvement of the right hip

Tuberculosis

Tuberculosis (TB) is a chronic granulomatous infection caused by the tubercule bacillus, either bovine (*Mycobacterium bovis*) or human (*Mycobacterium tuberculosis*). The former is acquired by drinking milk from infected cattle and the latter by 'droplet infection'. Immunocompromised patients carry an increased risk of TB.

1. **Primary TB** occurs in subjects not previously exposed to the bacillus. It is characterized by the 'primary complex' in the chest (Ghon focus + regional lymphadenopathy), which causes few if any symptoms and usually heals spontaneously.
2. **Post-primary TB** is the result of reinfection or recrudescence of a primary lesion, usually in a patient with impaired immunity. Clinical features include erythema nodosum, fibrocaseous pulmonary lesions and lymph node involvement (Fig. 20.103). Haematogenous spread (miliary TB) may involve many internal organs and bones (Fig. 20.104).
3. **Diagnostic tests**
   a. ***Sputum examination*** for acid-fast bacilli.
   b. ***Chest radiographs***.
   c. ***Tuberculin*** testing may be useful in the diagnosis of extrathoracic TB. A negative result usually excludes TB, whereas a positive result does not necessarily distinguish between previous exposure and active disease. This is because most individuals have already received Bacille Calmette-Guerin (BCG) and will therefore exhibit a hypersensitivity response.
   d. ***Anticord factor antibody*** is a new test for ocular TB.
4. **Treatment** is initially with at least three drugs (isoniazid, rifampicin, pyrazinamide or ethambutol) and then with isoniazid and rifampicin.
5. **Ophthalmic features**
   a. *Uncommon*. Granulomatous anterior uveitis, multifocal choroiditis and retinal periphlebitis.
   b. *Rare*. Solitary choroidal granulomas.

Tuberous sclerosis

Tuberous sclerosis (Bourneville disease) is a phacomatosis characterized by the triad of (a) *epilepsy*, (b) *mental retardation* and (c) *adenoma sebaceum*, although not all features are invariably present.

1. **Inheritance** is AD.
2. **Signs**
   a. *Skin*
   - Adenoma sebaceum, consisting of fibroangiomatous red papules with a butterfly distribution around the nose and cheeks, is universal (Fig. 20.105).
   - Ash leaf spots are hypopigmented patches on the trunk (Fig. 22.106), limbs and scalp. In infants with sparse skin pigmentation they are best detected using ultraviolet light, under which they fluoresce (Wood's lamp).

Fig. 20.105
Adenoma sebaceum in tuberous sclerosis

Fig. 20.106
Ash leaf spot in tuberous sclerosis

Fig. 20.107
Shagreen patches in tuberous sclerosis

Fig. 20.108
Extensive adenoma sebaceum and a fibrous plaque on the forehead in tuberous sclerosis

- Shagreen patches consist of diffuse thickening over the lumbar region (Fig. 20.107).
- Fibrous plaques on the forehead (Fig. 20.108).
- Skin tags (molluscum fibrosum pendulum).
- Café-au-lait spots.
- Subungual hamartomas (Fig. 20.109).

b. Neurological. Scattered astrocytic cerebral hamartomas are universal (Fig. 20.110).

c. Visceral hamartomas. Renal (angiomyolipomas) and cardiac (rhabdomyomas).

3. **Treatment** involves control of epilepsy and management of mental and behavioural disorder.
4. **Ophthalmic features**

a. Common. Retinal astrocytomas in 50%.

b. Uncommon. Hypopigmented spots on the iris and retina, papilloedema and sixth nerve palsy may develop due to raised intracranial pressure.

Fig. 20.109
Subungual hamartoma on the little toe in tuberous sclerosis

Fig. 20.110
Axial CT scan showing a periventricular astrocytic hamartoma (Courtesy of K. Nischal)

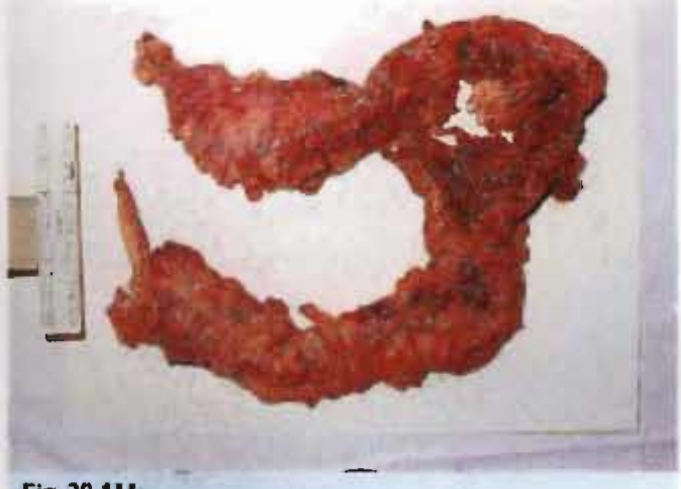

Fig. 20.111
Ulcerative colitis

Ulcerative colitis

Ulcerative colitis is an idiopathic, chronic, relapsing inflammatory disease, involving the rectum and extending proximally to involve part or all of the large intestine. The disease is characterized by diffuse surface ulceration of the mucosa with the development of crypt abscesses and pseudopolyps (Fig. 20.111). Patients with long-standing disease carry an increased risk of developing carcinoma of the colon.

1. **Presentation** is in the second to third decades with bloody diarrhoea, lower abdominal cramps, urgency and tenesmus. Constitutional symptoms include tiredness, weight loss, malaise and fever.
2. **Extra-intestinal signs**
   a. ***Mucocutaneous***. Oral aphthous ulceration, erythema nodosum and pyoderma gangrenosum.
   b. ***Skeletal***. Finger clubbing, asymmetrical lower limb arthritis, sacroiliitis and ankylosing spondylitis.
   c. ***Hepatic***. Autoimmune hepatitis, sclerosing cholangitis and cholangiocarcinoma.
   d. ***Vascular***. Arterial and venous thrombosis.
3. **Diagnostic tests**. Endoscopy and biopsy.
4. **Treatment** options include systemic steroids, sulphasalazine, immunosuppressive agents and colectomy.
5. **Ophthalmic features**
   a. ***Uncommon***. Acute anterior uveitis, peripheral corneal infiltrates and conjunctivitis.
   b. ***Rare***. Papillitis.

Vogt–Koyanagi–Harada syndrome

Vogt–Koyanagi–Harada (V-K-H) syndrome is an idiopathic, multisystem disorder which typically affects Hispanics, Japanese and pigmented individuals. Japanese patients have an increased prevalence of HLA-DR4 and Dw15. In practice, V-K-H can be subdivided into Vogt–Koyanagi disease, characterized mainly by skin changes and anterior uveitis, and Harada disease, in which neurological features and exudative retinal detachments predominate.

1. **Prodromal phase** lasting a few days is characterized by neurological and auditory manifestations.
   a. ***Meningitis*** causing headache and neck stiffness.
   b. ***Encephalopathy*** is less frequent and may manifest as convulsions, paresis and cranial nerve palsies.
   c. ***Auditory features*** include tinnitus, vertigo and deafness.
2. **Acute uveitic phase** follows soon thereafter and is characterized by bilateral granulomatous anterior or multifocal posterior uveitis and exudative retinal detachments.
3. **Convalescent phase** follows several weeks later and is characterized by:
   - Localized alopecia, poliosis and vitiligo (Fig. 20.112).
   - Focal depigmented fundus lesions (sunset glow fundus) and depigmented limbal lesions (Sugiura sign).
4. **Chronic–recurrent phase** is characterized by smouldering anterior uveitis with exacerbations.
5. **Diagnostic criteria** must include at least three of the following:
   - Bilateral chronic anterior uveitis.
   - Posterior uveitis, including exudative retinal detachment, disc swelling and 'sunset glow fundus'.
   - Neurological features.
   - Cutaneous lesions.
6. **Treatment** is with systemic steroids.

von Hippel–Lindau syndrome

von Hippel–Lindau syndrome is a life-threatening phacomatosis.

Fig. 20.112
Vitiligo in Vogt–Koyanagi–Harada syndrome

1. **Inheritance** is AD.
2. **Signs**
   a. Tumours
   - Haemangioblastomas of the cerebellum, spinal cord (Fig. 20.113), medulla or pons.
   - Renal carcinoma (Fig. 20.114) and phaeochromocytoma.

   b. Cysts. Renal, pancreatic, hepatic, epididymal, ovarian and pulmonary.
   c. Polycythaemia.
3. **Ophthalmic features.** Capillary haemangiomas of the retina or optic nerve head.

Fig. 20.114
Axial CT scan of the abdomen showing a large renal carcinoma in von Hippel–Lindau syndrome (Courtesy of G. Wilkinson)

Fig. 20.113
MRI scan showing a haemangioblastoma of the upper cervical cord in von Hippel–Lindau syndrome (Courtesy of D. Thomas)

Wegener granulomatosis

Wegener granulomatosis is an idiopathic, multisystem, granulomatous disorder characterized by generalized small-vessel vasculitis affecting predominantly the respiratory tract and the kidneys. It affects males more commonly than females.

1. **Presentation** is in the fifth decade, often with pulmonary symptoms.

Fig. 20.115
Chest radiograph showing cavitation in Wegener granulomatosis (Courtesy of S. Ghiacy)

2. Signs

a. Respiratory tract

- Upper respiratory tract involvement by necrotizing granulomatous inflammation may result in perforation of the nasal septum, saddle-shaped nasal deformity and nasal–paranasal fistulae.
- Lower respiratory tract involvement may result in nodular lesions, infiltrates and cavitation with fluid levels (Fig. 20.115).

b. Organs

- Necrotizing glomerulonephritis, with renal failure.
- Focal vasculitis involving the spleen, heart and adrenals.

c. Neurological. Polyneuritis and meningoencephalitis.

3. Diagnostic tests. Anti-neutrophil cytoplasm antibodies (c-ANCA) are found in over 90% of patients with active disease.

4. Treatment is with systemic steroids and cyclophosphamide.

5. Ophthalmic features

a. Common. Nasolacrimal obstruction and dacryocystitis.

b. Uncommon. Scleritis and peripheral ulcerative keratitis.

c. Rare. Orbital pseudo-tumour and occlusive retinal periarteritis.